Access DB# 104998

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jeffrey E. Russel Examiner #: 62785 Date: 10-1-2003
Art Unit: 1654 Phone Number 30 8-3975 Serial Number: 09/931,740
Mail Box and Bldg/Room Location: CM1-11D13 / CM1-9807 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Antineoplastic Conjugates Of Transferrin, Albumin And Polyethylene Glycol

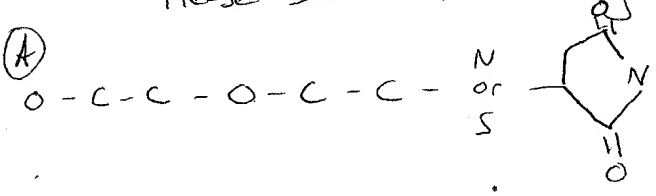
Inventors (please provide full names): F. Kratz

Earliest Priority Filing Date: 8-20-2001

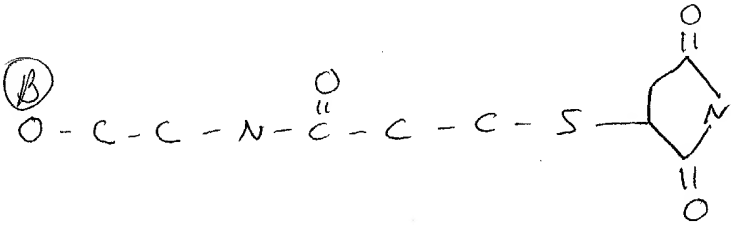
For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following partial structures:

(A)



(B)



Keywords are conjugate?, PEG, polyethylene glycol, link?, crosslink?

Thank you.

JER

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog

=> d his ful

FILE 'REGISTRY' ENTERED AT 17:03:11 ON 01 OCT 2003
L9 STR R5,DIS
L10 0 SEA SSS SAM L9
L11 4 SEA SSS FUL L9 Compd A - 4 hits (compds) in Reg. - see "dgne stat" for structure

FILE 'HCAPLUS' ENTERED AT 17:06:05 ON 01 OCT 2003
L12 5 SEA ABB=ON L11 Compd A - 5 cits in CA Plus

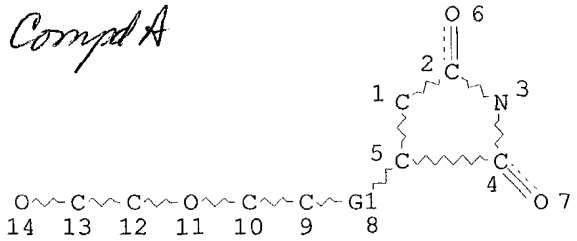
FILE 'REGISTRY' ENTERED AT 17:06:49 ON 01 OCT 2003
L13 STR
L14 9 SEA SSS SAM L13
L15 297 SEA SSS FUL L13 Compd B - 297 hits (compds) in Reg - see "dgne stat" for structure

FILE 'HCAPLUS' ENTERED AT 17:13:49 ON 01 OCT 2003
L16 107 SEA ABB=ON L15
L17 1 SEA ABB=ON L12 AND (?CONJUGAT? OR PEG OR ?POLYETHYLENE?(W)?GLY COL? OR ?LINK?) Compd A - 1 hit when combined with text terms - but
L18 48 SEA ABB=ON L16 AND (?CONJUGAT? OR PEG OR ?POLYETHYLENE?(W)?GLY COL? OR ?LINK?) Compd B - 48 hits when combined with text terms
L19 5 SEA ABB=ON L12 OR L17

I gave you all 5 with text terms highlighted

=> d que stat l19
L9 STR

Compd A



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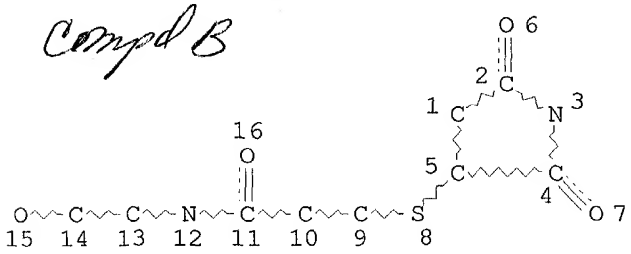
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L11 4 SEA FILE=REGISTRY SSS FUL L9
L12 5 SEA FILE=HCAPLUS ABB=ON L11
L17 1 SEA FILE=HCAPLUS ABB=ON L12 AND (?CONJUGAT? OR PEG OR ?POLYETHYLENE?(W)?GLYCOL? OR ?LINK?)
L19 5 SEA FILE=HCAPLUS ABB=ON L12 OR L17

=> d que stat l18
L13 STR

Compd B



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

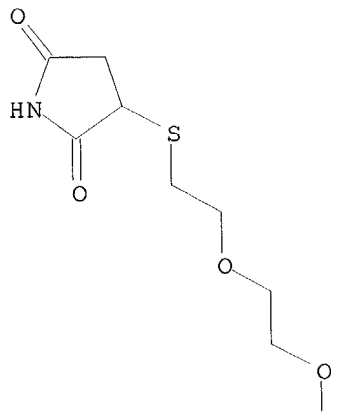
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L15 297 SEA FILE=REGISTRY SSS FUL L13
L16 107 SEA FILE=HCAPLUS ABB=ON L15
L18 48 SEA FILE=HCAPLUS ABB=ON L16 AND (?CONJUGAT? OR PEG OR ?POLYETHYLENE?(W)?GLYCOL? OR ?LINK?)

=> d ibib abs hitstr l19 1-5

L19 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:242945 HCAPLUS
DOCUMENT NUMBER: 131:72399
TITLE: Multivalent Thioether-Peptide **Conjugates**: B Cell Tolerance of an Anti-Peptide Immune Response
AUTHOR(S): Jones, David S.; Coutts, Stephen M.; Gamino, Christina A.; Iverson, G. Michael; Linnik, Matthew D.; Randow, Martina E.; Ton-Nu, Huong-Thu; Victoria, Edward J.
CORPORATE SOURCE: La Jolla Pharmaceutical Company, San Diego, CA, 92121, USA
SOURCE: Bioconjugate Chemistry (1999), 10(3), 480-488
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antibodies which bind .beta.2-glycoprotein I (.beta.2GPI) are assocd. with antiphospholipid syndrome. Synthetic peptide mimotopes have been discovered which compete with .beta.2GPI for binding to selected anti-.beta.2GPI. A thiol-contg. **linker** was attached to the N-terminus of two cyclic thioether peptide mimotopes, peptides 1a and 1b. The resulting peptides, with **linker** attached, were reacted with two different haloacetylated platforms to prep. four tetravalent peptide-platform **conjugates** to be tested as B cell toleragens. The **linker**-contg. peptides were reacted with maleimide-derivatized keyhole limpet hemocyanin (KLH) to provide peptide-KLH **conjugates**. Peptides 1a and 1b were also modified by acylation with 3-(4'-hydroxyphenyl)propionic acid N-hydroxysuccinimidyl ester. The resulting hydroxyphenyl peptides were radioiodinated and used to measure anti-peptide antibody levels. The KLH **conjugates** were used to immunize mice to generate an anti-peptide immune response. The immunized mice were treated with the **conjugates** or saline soln. and boosted with the appropriate peptide-KLH **conjugate**. Three of the four **conjugates** suppressed the formation of anti-peptide antibody. The stabilities of the **conjugates** in mouse serum were measured, and the relative stabilities did not correlate with ability to suppress antibody formation.
IT **228403-78-9DP, conjugates** with keyhole limpet hemocyanin
228403-79-0DP, conjugates with keyhole limpet hemocyanin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of; multivalent thioether-peptide **conjugates** in relation to B-cell tolerance)
RN 228403-78-9 HCAPLUS
CN L-Cysteinamide, N-[[2-[2-[2-[(2,5-dioxo-3-pyrrolidinyl)thio]ethoxy]ethoxy]ethoxy]acetyl]glycyl-L-prolyl-L-homocysteinyl-L-isoleucyl-L-leucyl-L-leucyl-L-alanyl-2-methyl-L-prolyl-L-.alpha.-aspartyl-L-arginyl-, cyclic (3.fwdarw.11)-thioether (9CI) (CA INDEX NAME)

PAGE 1-A



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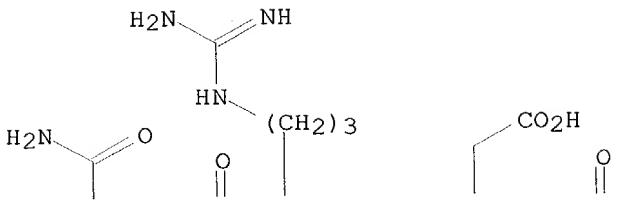

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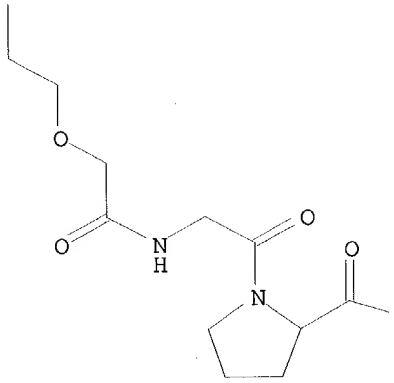

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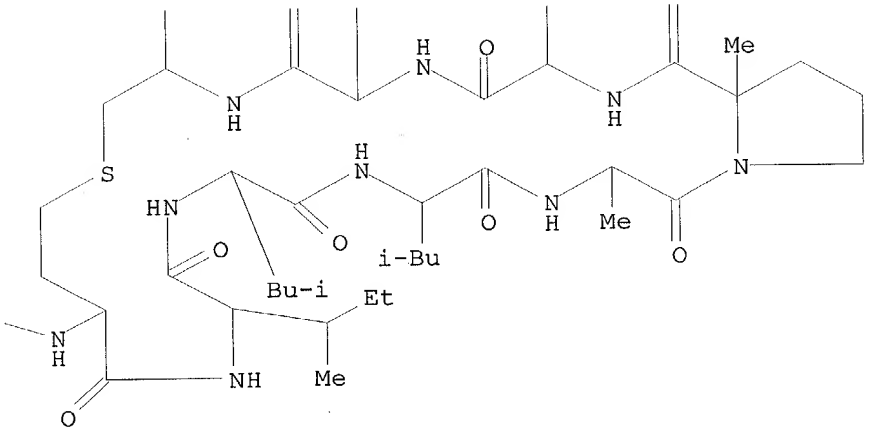

RN 228403-79-0 HCAPLUS
CN L-Cysteinamide, N-[[2-[2-[2-[(2,5-dioxo-3-pyrrolidinyl)thio]ethoxy]ethoxy]ethoxy]acetyl]glycyl-L-prolyl-L-homocysteinyl-L-isoleucyl-L-leucyl-L-leucyl-L-alanyl-L-arginyl-L-.alpha.-aspartyl-L-arginyl-, cyclic (3.fwdarw.11)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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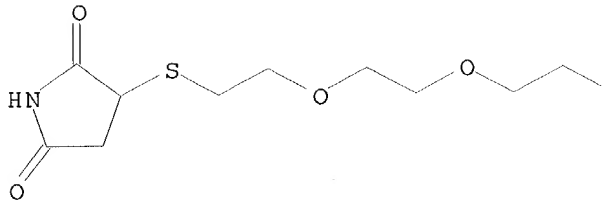

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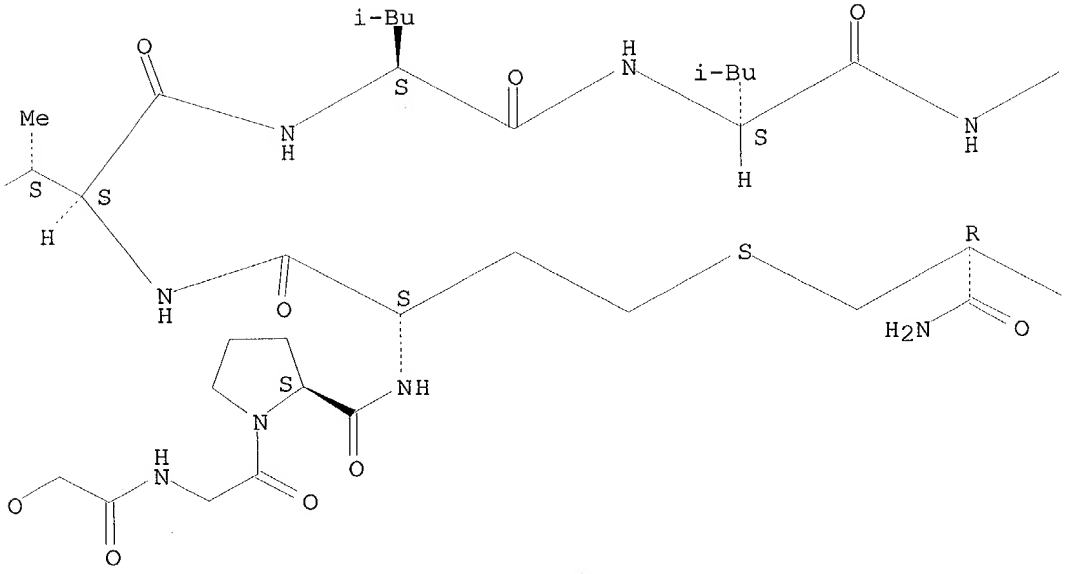
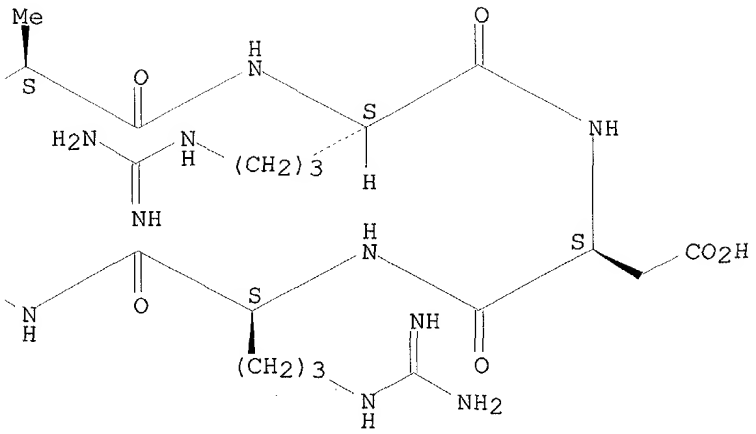




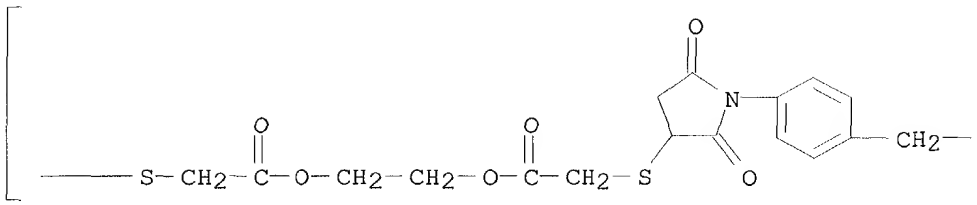
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:106107 HCAPLUS
DOCUMENT NUMBER: 84:106107
TITLE: Polyimidothioethers
AUTHOR(S): Crivello, James V.
CORPORATE SOURCE: Res. Dev. Cent., Gen. Electr. Co., Schenectady, NY, USA
SOURCE: Journal of Polymer Science, Polymer Chemistry Edition (1976), 14(1), 159-81
CODEN: JPLCAT; ISSN: 0449-296X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Michael condensation polymn. of bismaleimide compds. with H2S or bisthiols in the presence of a proton donor to inhibit anionic polymn. gave sol. polyimidothioethers. Some of the polymers had high m.p.'s and 1 polymer, i.e. N,N'-bismaleimido-4,4'-diphenylmethane-H2S copolymer [39664-71-6], resisted rapid degrdn. at .ltoreq.500.degree. in N and in air. Model compds. were also prepd.

IT **39989-70-3**
RL: USES (Uses)
(sol.)
RN 39989-70-3 HCAPLUS
CN Poly[(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenemethylene-1,4-phenylene(2,5-dioxo-1,3-pyrrolidinediyl)thio(2-oxo-1,2-ethanediyl)oxy-1,2-ethanediyloxy(1-oxo-1,2-ethanediyl)thio] (9CI) (CA INDEX NAME)

PAGE 1-A



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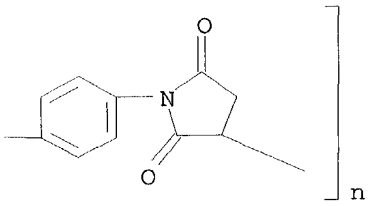
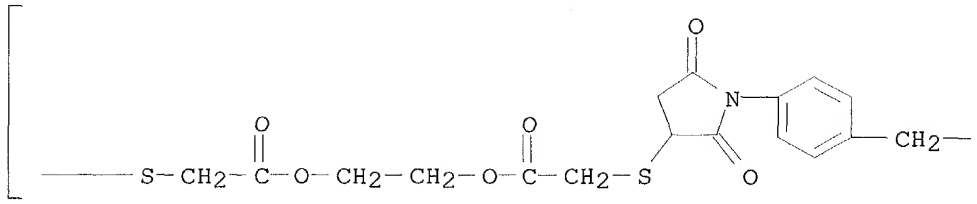


L19 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:438194 HCAPLUS
DOCUMENT NUMBER: 81:38194
TITLE: Poly(imidothio ethers)
AUTHOR(S): Crivello, J. V.
CORPORATE SOURCE: Gen. Electr. Corp. Res. Dev., Schenectady, NY, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1972), 13(2), 924-9
CODEN: ACPPAY; ISSN: 0032-3934
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Poly(imido sulfide) resins (18) were prepd. by condensation of a bismaleimide with H2S or a bismercaptan; the reactions were rapid and exothermic in common org. solvents. In an example, 1:5 H2S-N mixt. was bubbled 2 hrs through 5 g N,N'-bismaleimido-4,4'-diphenylmethane in 50 ml DMF-AcOH at 25.deg. to give the poly(imido sulfide) (I) [39989-81-6] of intrinsic viscosity 0.53 dl/g(DMF, 25.deg.) and m.p. 271-5.deg.. The model reaction, Michael condensation of H2S with N-phenylmaleimide [941-69-5], was also discussed.

IT **39989-70-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 39989-70-3 HCAPLUS
CN Poly[(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenemethylene-1,4-phenylene(2,5-dioxo-1,3-pyrrolidinediyl)thio(2-oxo-1,2-ethanediyl)oxy-1,2-ethanediyloxy(1-oxo-1,2-ethanediyl)thio] (9CI) (CA INDEX NAME)

PAGE 1-A



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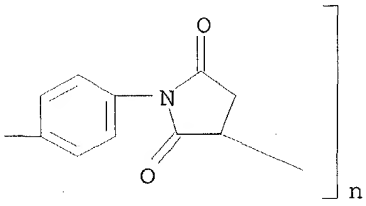


L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:137042 HCAPLUS
DOCUMENT NUMBER: 78:137042
TITLE: Polyimides
INVENTOR(S): Crivello, James Vincent
PATENT ASSIGNEE(S): General Electric Co.
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2234148	A1	19730125	DE 1972-2234148	19720712
US 3741942	A	19730626	US 1971-163411	19710716
GB 1392725	A	19750430	GB 1972-27664	19720613
CA 982737	A1	19760127	CA 1972-145762	19720627
BE 786121	A1	19721103	BE 1972-119729	19720711
FR 2146254	A1	19730302	FR 1972-25149	19720711
AT 321580	B	19750410	AT 1972-6046	19720713
NL 7209827	A	19730118	NL 1972-9827	19720714
IT 965073	A	19740131	IT 1972-27041	19720715
BR 7204747	A0	19730531	BR 1972-4747	19720717

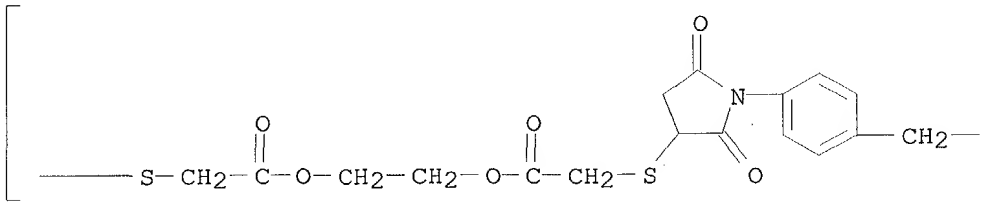
PRIORITY APPLN. INFO.: US 1971-163411 19710716

AB The polyimides I (R1, R2 = divalent radicals) are prepd. by soln. or emulsion polymn. of dimaleimides with disulfides. Thus, stirring 7.16 g N,N'-(methylenedi-p-phenylene)dimaleimide 4.2 g ethylene glycol bis(mercaptoacetate), 50 ml cresol, and 2 drops Bu3N 3 hr at room temp. gives 11.9 g ethylene glycol bis(mercaptoacetate)-N,N'-(methylenedi-p-phenylene)dimaleimide copolymer (I, R1 = methylenedi-p-phenylene, R2 = CH2CH2CO2CH2CH2O2CCH2) [39708-62-8], softening point 160-70.deg., cut-through temp. .sim. 160.deg..

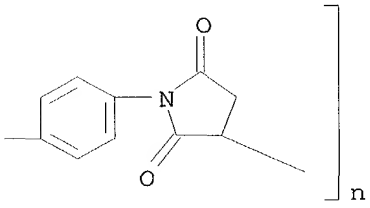
IT **39989-70-3P**

RL: PREP (Preparation)
(prepn. of)
RN 39989-70-3 HCAPLUS
CN Poly[(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenemethylene-1,4-phenylene(2,5-dioxo-1,3-pyrrolidinediyl)thio(2-oxo-1,2-ethanediyl)oxy-1,2-ethanediyloxy(1-oxo-1,2-ethanediyl)thio] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L19 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:111952 HCAPLUS
DOCUMENT NUMBER: 78:111952
TITLE: Polyimides
INVENTOR(S): Crivello, James Vincent
PATENT ASSIGNEE(S): General Electric Co.
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2234149	A1	19730125	DE 1972-2234149	19720712
US 3766138	A	19731016	US 1971-163410	19710716
GB 1392628	A	19750430	GB 1972-27666	19720613
CA 982736	A1	19760127	CA 1972-145761	19720627
BE 786120	A1	19721103	BE 1972-119728	19720711
FR 2146253	A1	19730302	FR 1972-25148	19720711
AT 321581	B	19750410	AT 1972-6047	19720713
NL 7209825	A	19730118	NL 1972-9825	19720714
IT 962887	A	19731231	IT 1972-27039	19720715
US 3855239	A	19741217	US 1973-325065	19730119

PRIORITY APPLN. INFO.: US 1971-163410 19710716
AB Polyimides are prepd. by polymn. of the maleimide derivs. I (R1, R2 = divalent radicals) with H2S or disulfides in the presence of proton-donor

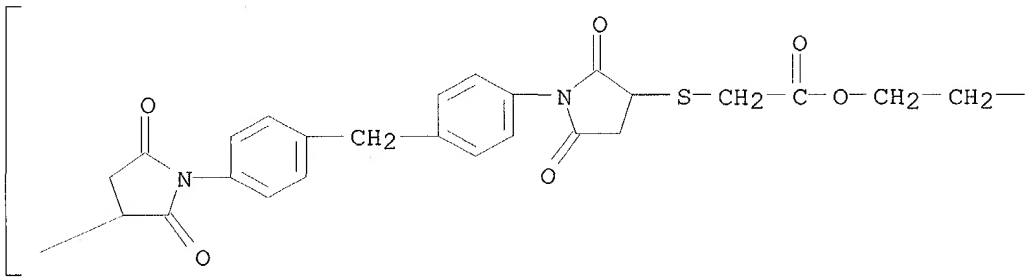
catalysts. Thus, refluxing 3.96 g 4,4'-diaminodiphenylmethane [101-77-9], 14.3 g N,N'-(methylenedi-p-phenylene)dimaleimide [13676-54-5], and 200 ml HOAc 2 hr gives 18.1 g 3,3'-[(methylenedi-p-phenylene)diimino]bis[N-[p-(maleimidobenzyl)phenyl]succinimide] (I, R1 = R2 = methylenedi-p-phenylene)(II) [39664-22-7]. Passing 1 l./hr H2S through a soln. of 5 g II and 2 drops tetramethylethylenediamine in 50 ml cresol 1 hr at 58.deg. gives hydrogen sulfide-3,3'-[(methylenedi-p-phenylene)diimino]bis[N-[p-(p-maleimidobenzyl)phenyl]succinimide]copolymer [39664-70-5], intrinsic viscosity 0.58 dl/g.

IT **39989-76-9P**
RL: PREP (Preparation)
(prepn. of)

RN 39989-76-9 HCAPLUS

CN Poly[(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenemethylene-1,4-phenylene(2,5-dioxo-1,3-pyrrolidinediyl)thio(2-oxo-1,2-ethanediyl)oxy-1,2-ethanediyloxy(1-oxo-1,2-ethanediyl)thio(2,5-dioxo-3,1-pyrrolidinediyl)-1,4-phenylenemethylene-1,4-phenylene(2,5-dioxo-1,3-pyrrolidinediyl)imino-1,4-phenyleneoxy-1,4-phenyleneimino] (9CI) (CA INDEX NAME)

PAGE 1-A



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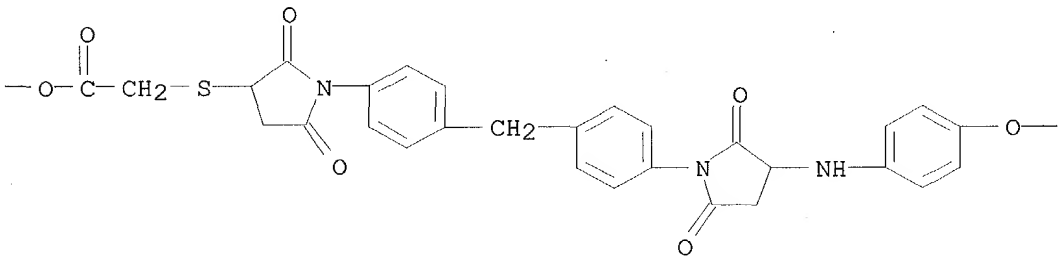

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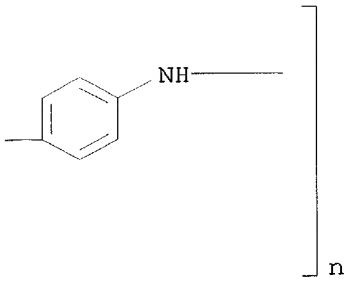


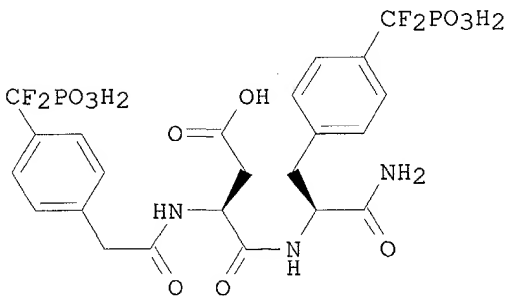
=> d ibib abs l18 1-48

L18 ANSWER 1 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:396733 HCAPLUS
DOCUMENT NUMBER: 138:396226
TITLE: Combinatorial library-based protein tyrosine phosphatase 1B (PTP1B) inhibitor and ligand discovery
INVENTOR(S): Zhang, Zhong-Yin; Lawrence, David S.
PATENT ASSIGNEE(S): Albert Einstein College of Medicine of Yeshiva University, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003041729	A1	20030522	WO 2002-US30492	20020926

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-325009P P 20010926
OTHER SOURCE(S): MARPAT 138:396226
GI



I

AB Methods for discovery of enzyme ligands and inhibitors are disclosed. The methods comprise the creation and testing of combinatorial libraries comprising an active site-targeted component, a **linker** component and a peripheral site-targeted component. The methods also comprise a novel assay for detg. whether a compd. is a ligand of an enzyme. The assay evaluates whether the compd. can inhibit the binding of a known ligand of the active site of the enzyme to a mutant of the enzyme that can

bind the enzyme substrate but cannot catalyze an enzymic reaction with the substrate. Various ligands and inhibitors of protein tyrosine phosphatase 1B (PTP1B) are also disclosed. These ligands and inhibitors were discovered using the above methods. One particular inhibitor (I) discovered using the invention methods has the highest specificity and affinity of any PTP1B inhibitor discovered to date. The inhibitors of the invention may serve as effective therapeutics for the treatment of type II diabetes and obesity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:129325 HCAPLUS
DOCUMENT NUMBER: 138:193258
TITLE: Methods of imaging and treatment with targeted compositions
INVENTOR(S): Unger, Evan C.; Wu, Yunqiu
PATENT ASSIGNEE(S): Bristol-Myers Squibb Medical Imaging, Inc., USA
SOURCE: U.S., 96 pp., Cont.-in-part of U.S. Ser. No. 218,660. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6521211	B1	20030218	US 1999-243640	19990203
CN 1187137	A	19980708	CN 1996-194499	19960606
CN 1083280	B	20020424		
WO 2000045856	A2	20000810	WO 2000-US2620	20000202
WO 2000045856	A3	20010215		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1146911	A2	20011024	EP 2000-914480	20000202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2003157025	A1	20030821	US 2003-341167	20030113

PRIORITY APPLN. INFO.:
US 1995-497684 B2 19950607
US 1996-640464 B2 19960501
US 1996-660032 B2 19960606
US 1998-73913P P 19980206
US 1998-218660 A2 19981222
US 1999-243640 A 19990203
WO 2000-US2620 W 20000202

AB The invention concerns novel ultrasound methods comprising administering to a patient a targeted vesicle compn. which comprises vesicles comprising a lipid, protein or polymer, encapsulating a gas, in combination with a targeting ligand, and scanning the patient using ultrasound. The scanning may comprise exposing the patient to a first type of ultrasound energy and then interrogating the patient using a second type of ultrasound energy. The targeting ligand preferably targets tissues, cells or receptors, including myocardial cells, endothelial cells, epithelial cells, tumor

cells and the glycoprotein GPIIbIIIa receptor. The methods may be used to detect a thrombus, enhancement of an old or echogenic thrombus, low concns. of vesicles and vesicles targeted to tissues, cells or receptors.
REFERENCE COUNT: 546 THERE ARE 546 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:540254 HCAPLUS
DOCUMENT NUMBER: 137:99024
TITLE: Use of somatostatin analogs for the delivery of anti-tumor drugs to tumor cells
INVENTOR(S): Chen, Shui-tein; Wu, Ying-ta; Huang, Chun-ming
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 482,451, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094964	A1	20020718	US 2000-734298	20001211
US 6552007	B2	20030422		

PRIORITY APPLN. INFO.: US 2000-482451 B2 20000113
OTHER SOURCE(S): MARPAT 137:99024
AB A **conjugate** of somatostatin-spacer-drug and a method of making the same are given. The **conjugate** can be used to enhance an anti-cancer drug's specificity on the targeted tumor cells, thus increasing its therapeutic efficacy while reducing side-effects. Paclitaxel-glutaryl-octreotide was prepd. from paclitaxel, glutaric anhydride and solid-phase peptide synthesis of octreotide. Octreotide-**conjugated** paclitaxel induced only the death of MCF-7 cells but not CHO cells.

L18 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:124091 HCAPLUS
DOCUMENT NUMBER: 136:369989
TITLE: Characterizing closely spaced, complex disulfide bond patterns in peptides and proteins by liquid chromatography/electrospray ionization tandem mass spectrometry
AUTHOR(S): Yen, Ten-Yang; Yan, Hui; Macher, Bruce A.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, San Francisco State University, San Francisco, CA, 94132, USA
SOURCE: Journal of Mass Spectrometry (2002), 37(1), 15-30
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Identifying the Cys residues involved in disulfide **linkages** of peptides and proteins that contain complex disulfide bond patterns is a significant anal. challenge. This is esp. true when the Cys residues involved in the disulfide bonds are closely spaced in the primary sequence. Peptides and proteins that contain free Cys residues located near disulfide bonds present the addnl. problem of disulfide shuffling via the thiol-disulfide exchange reaction. In this paper, we report a

convenient method to identify complex disulfide patterns in peptides and proteins using liq. chromatog./electrospray ionization tandem mass spectrometry (LC/ESI-MS/MS) in combination with partial redn. by tris(2-carboxyethyl)phosphine (TCEP). The method was validated using well-characterized peptides and proteins including endothelin, insulin, .alpha.-conotoxin SI and IgG (IgG2a, mouse). Peptide or protein digests were treated with TCEP in the presence of an alkylation reagent, maleimide-biotin (M-biotin) or N-ethylmaleimide (NEM), followed by complete redn. with dithiothreitol and alkylation by iodoacetamide (IAM). Subsequently, peptides that contained alkylated Cys were analyzed by capillary LC/ESI-MS/MS to det. which Cys residues were modified with M-biotin/NEM or IAM. The presence of the alkylating reagent (M-biotin or NEM) during TCEP redn. was found to minimize the occurrence of the thiol-disulfide exchange reaction. A crit. feature of the method is the stepwise redn. of the disulfide bonds and the orderly, sequential use of specific alkylating reagents.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:6343 HCAPLUS
DOCUMENT NUMBER: 136:82299
TITLE: A reagent and method for incorporation of phosphorylation sites
INVENTOR(S): Inglese, James; Glickman, Joseph Fraser
PATENT ASSIGNEE(S): Pharmacopeia, Inc., USA
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

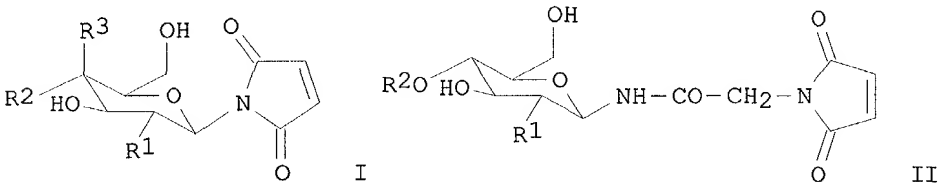
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6335176	B1	20020101	US 1998-174216	19981016

PRIORITY APPLN. INFO.: US 1998-174216 19981016
OTHER SOURCE(S): MARPAT 136:82299
AB A reagent is described for incorporating phosphorylation sites into compds., particularly into proteins and peptides. The reagent has the structure A-B-C wherein A is a moiety that is specifically reactive with a reactive side chain in the compd., B is a **linking** moiety, and C is a peptide sequence that contains a kinase substrate. Protein kinase A substrate peptide AcNHCSRRASVYNH2 (peptide A) was reacted with succinimidyl 6-((iodoacetyl)amino)hexanoate to make a reagent that was reacted with various peptides and proteins (e.g., neurokinin A, interleukin 8, leptin, etc.). The peptide A **conjugates** were phosphorylated and studied with their receptors.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:671360 HCAPLUS
DOCUMENT NUMBER: 136:299552
TITLE: Coupling of nuclear localization signals to plasmid DNA
AUTHOR(S): Neves, Carole; Scherman, Daniel; Wils, Pierre
CORPORATE SOURCE: UMR7001 Aventis/CNRS/ENSCP, Aventis Pharma, Vitry-sur-Seine, Fr.
SOURCE: Methods in Molecular Medicine (2001), 65(Nonviral

Vectors for Gene Therapy), 105-109
CODEN: MMMEFN
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review on the methodol. for covalently assocg. nuclear localization signal (NLS) peptides to DNA, in which cationic NLS peptides are covalently bound to plasmid DNA (pDNA) by photoactivation. A new chem. strategy for covalent coupling of NLS peptides to pDNA is described. P-azidotetrafluorobenzyl-NLS peptide **conjugate** was synthesized and used to covalently assoc. NLS peptides to pDNA by photoactivation.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:102214 HCAPLUS
DOCUMENT NUMBER: 134:281112
TITLE: Chemoselective ligation of maleimidosugars to peptides/protein for the preparation of neoglycopeptides/neoglycoprotein
AUTHOR(S): Shin, I.; Jung, H.-j.; Lee, M.-r.
CORPORATE SOURCE: Department of Chemistry, Yonsei University, Seoul, 120-749, S. Korea
SOURCE: Tetrahedron Letters (2001), 42(7), 1325-1328
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:281112
GI



AB Two types of maleimidosugars as thiol-selective carbohydrates, 1-maleimidosugars I (R1 = NHAc, R2 = OH, R3 = H; R1 = OH, R2 = H, R3 = OH; R1 = OH, R2 = .alpha.-D-glucosyl-O-, R3 = H) and acetyl-**linked** maleimidosugars II (R1 = NHAc, R2 = H; R1 = OH, R2 = .beta.-D-galactosyl; R1 = OH, R2 = .beta.-D-glucosyl), were efficiently synthesized. They were chemoselectively coupled to a cysteine residue belonging to glutathione, Fas peptide and bovine serum albumin (BSA) to prep. the corresponding glycopeptides and glycoprotein with stable thioether **linkages**.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:95555 HCAPLUS
DOCUMENT NUMBER: 135:13817
TITLE: Enhancement of gene delivery by an analogue of .alpha.-MSH in a receptor-independent fashion
AUTHOR(S): Chluba, J.; Lima de Souza, D.; Frisch, B.; Schuber, F.
CORPORATE SOURCE: Laboratoire de Chimie Bioorganique, UMR 7514 CNRS-ULP,

Faculte de Pharmacie, Illkirch, 67400, Fr.
SOURCE: Biochimica et Biophysica Acta (2001), 1510(1-2), 198-208
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to transfect melanoma specifically by receptor-mediated endocytosis we prepd. dioctadecyl aminoglycylspermine (lipospermine)-DNA complexes with [Nle4,D-Phe7]-.alpha.-MSH(4-10), a pseudo-peptide analog of .alpha.-MSH (.alpha.-MSH) **linked** to a thiol-reactive phospholipid. With these complexes we obtained an up to 70-fold increase of transfection with B16-F1 melanoma cells. However when B16-G4F, an .alpha.-MSH receptor neg. melanoma cell line was transfected, an up to 700-fold increased transfection efficiency was obsd. The peptide hormone analog was equally efficient when it was only mixed with lipospermine-DNA complexes without covalent coupling. In addn. to melanoma cells we also obtained up to 30-fold increased transfection with BN cells (embryonic liver cells). Our data show that an .alpha.-MSH analog increased transfection independently of the MSH receptor expression but reaches efficiencies approaching those obtained with peptides derived from viral fusion proteins. The absence of targeting of constructs contg. [Nle4,D-Phe7]-.alpha.-MSH(4-10) can probably be attributed due to the relatively modest no. of MSH receptors at the surface of melanoma. We suggest, however, that the peptide hormone analog used in this study has membrane-active properties and could be of interest as helper agent to enhance non-viral gene delivery presumably by endosomal-destabilizing properties.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:755211 HCAPLUS
DOCUMENT NUMBER: 133:340208
TITLE: Novel compositions useful for delivering anti-inflammatory agents into a cell
INVENTOR(S): Unger, Evan C.; McCreery, Thomas; Sadewasser, David A.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046394	A2	20001025	EP 2000-303249	20000418
EP 1046394	A3	20011010		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-294623 A 19990419
AB The present invention is directed, inter alia, to compns. and their use for delivering compds. into a cell. In a preferred embodiment, the compns. comprise, in combination with the compd. to be delivered, an org. halide, a targeting ligand, and a nuclear localization sequence, optionally in the presence of a carrier. Ultrasound may be applied, if desired. The compns. are particularly suitable for the treatment of inflammatory diseases.

L18 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:573678 HCAPLUS
DOCUMENT NUMBER: 133:172215
TITLE: Controlling protein levels in eucaryotic organisms using novel compds. comprising a ubiquitination recognition element and a protein binding element
INVENTOR(S): Kenten, John H.; Roberts, Steven F.; Lebowitz, Michael S.
PATENT ASSIGNEE(S): Proteinix, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047220	A1	20000817	WO 2000-US3436	20000211
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6306663	B1	20011023	US 1999-406781	19990928
EP 1156817	A1	20011128	EP 2000-908580	20000211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002536417	T2	20021029	JP 2000-598172	20000211
US 2002146843	A1	20021010	US 2001-880149	20010614
US 2002173049	A1	20021121	US 2001-880132	20010614
US 6559280	B2	20030506		
US 2003153727	A1	20030814	US 2003-345281	20030116

PRIORITY APPLN. INFO.:
US 1999-119851P P 19990212
US 1999-406781 A2 19990928
WO 2000-US3436 W 20000211
US 2001-880132 A3 20010614

AB The invention relates to novel compds. comprising a ubiquitination recognition element and a protein binding element. The invention also relates to the use of said compds. for modulating the level and/or activity of a target protein. The compds. are useful for the treatment of diseases such as infections, inflammatory conditions, cancer and genetic diseases. The compds. are also useful as insecticides and herbicides.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:454201 HCAPLUS
DOCUMENT NUMBER: 133:70819
TITLE: Thrombus imaging agents
INVENTOR(S): Dean, Richard T.; Lister-James, John
PATENT ASSIGNEE(S): Diatide, Inc., USA
SOURCE: U.S., 27 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6083481	A	20000704	US 1998-141127	19980827

PRIORITY APPLN. INFO.: US 1998-141127 19980827

AB This invention relates to radiolabeled reagents that are scintigraphic imaging agents for imaging sites of thrombus formation in vivo, and methods for producing such reagents. Specifically, the invention relates to reagents each comprised of a specific binding compd., capable of binding to at least one component of a thrombus, covalently **linked** to a radiolabel-binding moiety. The invention provides these reagents, methods and kits for making such reagents, and methods for using such reagents labeled with technetium-99m to image thrombus sites in a mammalian body.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:351544 HCAPLUS
DOCUMENT NUMBER: 133:9081
TITLE: Modified and truncated penetratin derivatives as membrane translocation carriers for drug transport
INVENTOR(S): Fischer, M. Peter; Zhelev, Nikolai
PATENT ASSIGNEE(S): Cyclacel Limited, UK
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029427	A2	20000525	WO 1999-GB3750	19991111
WO 2000029427	A3	20001005		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2346616	A1	20000816	GB 1999-26719	19991111
EP 1135410	A2	20010926	EP 1999-954212	19991111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002530059	T2	20020917	JP 2000-582414	19991111
US 2002098236	A1	20020725	US 2001-854204	20010511

PRIORITY APPLN. INFO.:

GB 1998-25000	A	19981113
GB 1998-25001	A	19981113
GB 1999-2522	A	19990204
GB 1999-2525	A	19990204
GB 1999-14578	A	19990622
WO 1999-GB3750	W	19991111
US 1999-438460	A3	19991112

AB The invention relates to modified and truncated forms of the membrane

transport vector penetratin, a peptide comprising residues 45-58 of the Antennapedia homeodomain protein. Such truncated forms include 7-mer peptides that may in themselves include further variation. Such smaller or truncated forms of penetratin are advantageous in that they are more acceptable to the pharmaceutical industry as delivery carrier moieties, by virtue of the carrier-cargo **conjugate** having an advantageous immunogenicity, soly., and clearance, and in some cases advantageous efficacy as compared to using a **conjugate** comprised of full length penetratin. Carrier moieties are synthetically **linked** to a cargo moiety selected from p21WAF-derived peptides, p16-derived peptides or the drugs roscovitine, taxol, or a podophyllotoxin. The truncated penetratin-podophyllotoxin **conjugate**, for example, is more effective in terms of anti-proliferative activity on tumor cells while exhibiting lower generalized toxicity.

L18 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:288434 HCAPLUS
DOCUMENT NUMBER: 133:135577
TITLE: The total synthesis of SB-238592, a 1,6-bis(succinimido)hexane cross-**linked** decapeptide homodimeric bradykinin B2 antagonist, by solution-phase chemistry
AUTHOR(S): Blodgett, James K.; Califano, Jean-C.; Shao, Jun; Tolle, John C.; Chang, Wen-S.
CORPORATE SOURCE: Department of Process Research, Chemical and Agricultural Products Division, Abbott Laboratories, North Chicago, IL, 60064-4000, USA
SOURCE: Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 196-197. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. A soln.-phase approach to SB-238592, Bradycor, based on minimal amino acid side-chain protection is reported.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:34769 HCAPLUS
DOCUMENT NUMBER: 132:93654
TITLE: Preparation of peptide derivatives for improved delivery of drug therapeutic agents
INVENTOR(S): Fischer, Peter Martin; Wang, Shudong
PATENT ASSIGNEE(S): Cyclacel Limited, UK
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001417	A1	20000113	WO 1999-GB1957	19990622

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2333145	AA	20000113	CA 1999-2333145	19990622	
AU 9945198	A1	20000124	AU 1999-45198	19990622	
AU 756014	B2	20030102			
GB 2340121	A1	20000216	GB 1999-14577	19990622	
GB 2340121	B2	20000906			
EP 1093383	A1	20010425	EP 1999-928071	19990622	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002519392	T2	20020702	JP 2000-557863	19990622	
US 6472507	B1	20021029	US 1999-346847	19990702	
US 2003119735	A1	20030626	US 2002-210660	20020731	

PRIORITY APPLN. INFO.:
GB 1998-14527 A 19980703
WO 1999-GB1957 W 19990622
US 1999-346847 A1 19990702

AB The present invention relates to a novel drug delivery system for use in the improved delivery of drug therapeutic agents into target cells. The system comprises a drug moiety **linked** to a carrier moiety wherein the carrier moiety comprises a homeobox peptide or its fragment or deriv. Thus, {[4-[N-(2,4-diamino-6-pteridinylmethyl)-N-methylamino]benzoyl]-Glu-Gly-.beta.-Ala}4-Lys2-Lys-.beta.-Ala-Arg-Gln-Ile-Lys-Ile-Trp-Phe-Gln-Asn-Arg-Arg-Met-Lys-Trp-Lys-Lys-OH was prepd. by the solid-phase method and assayed for in vitro cytotoxicity.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:9442 HCAPLUS
DOCUMENT NUMBER: 132:170955
TITLE: Acid-sensitive **polyethylene glycol conjugates** of doxorubicin: preparation, in vitro efficacy and intracellular distribution
AUTHOR(S): Rodrigues, Paula C. A.; Beyer, Ulrich; Schumacher, Peter; Roth, Thomas; Fiebig, Heinz H.; Unger, Clemens; Messori, Luigi; Orioli, PierLuigi; Paper, Dietrich H.; Mulhaupt, Rolf; Kratz, Felix
CORPORATE SOURCE: Department of Medical Oncology, Clinical Research, Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(11), 2517-2524
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Coupling anticancer drugs to synthetic polymers is a promising approach of enhancing the antitumor efficacy and reducing the side-effects of these agents. Doxorubicin maleimide derivs. contg. an amide or acid-sensitive hydrazone **linker** were therefore coupled to .alpha.-methoxy-poly(ethylene glycol)-thiopropionic acid amide (MW 20000 Da), .alpha.,.omega.-bis-thiopropionic acid amide poly(ethylene glycol) (MW 20000 Da) or .alpha.-tert-butoxy-poly(ethylene glycol)-thiopropionic acid amide (MW 70000 Da) and the resulting **polyethylene glycol** (**PEG**) **conjugates** isolated through size-exclusion chromatog. The polymer drug derivs. were designed as to release doxorubicin inside the tumor cell by acid-cleavage of the hydrazone bond after uptake of the **conjugate** by endocytosis.

The acid-sensitive **PEG conjugates** contg. the carboxylic hydrazone bonds exhibited in vitro activity against human BXF T24 bladder carcinoma and LXFL 529L lung cancer cells with IC70 values in the range 0.02-1.5 .mu.m (cell culture assay: propidium iodide fluorescence or colony forming assay). In contrast, **PEG** doxorubicin **conjugates** contg. an amide bond between the drug and the polymer showed no in vitro activity. Fluorescence microscopy studies in LXFL 529 lung cancer cells revealed that free doxorubicin accumulates in the cell nucleus whereas doxorubicin of the acid-sensitive **PEG** doxorubicin **conjugates** is primarily localized in the cytoplasm. Nevertheless, the acid-sensitive **PEG** doxorubicin **conjugates** retain their ability to bind to calf thymus DNA as shown by fluorescence and visible spectroscopy studies. Results regarding the effect of an acid-sensitive **PEG conjugate** of mol. wt. 20000 in the chorioallantoic membrane (CAM) assay indicate that this **conjugate** is significantly less embryotoxic than free doxorubicin although antiangiogenic effects were not obsd.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:578886 HCAPLUS
DOCUMENT NUMBER: 132:666
TITLE: Dimers of bradykinin and substance P antagonists as potential anti-cancer drugs
AUTHOR(S): Stewart, J. M.; Gera, L.; Chan, D. C.
CORPORATE SOURCE: Department of Biochemistry, University of Colorado Medical School, Denver, CO, 80262, USA
SOURCE: Peptide Science: Present and Future, Proceedings of the International Peptide Symposium, 1st, Kyoto, Nov. 30-Dec. 5, 1997 (1999), Meeting Date 1997, 731-732. Editor(s): Shimonishi, Yasutsugu. Kluwer: Dordrecht, Neth.
CODEN: 68BYA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors report dimers of bradykinin (BK) and substance P (SP) antagonists and heterodimers of SP and BK antagonists that are potent selectively cytotoxic agents for small cell lung cancer (SCLC). Although straight-chain analogs of SP and bombesin have shown toxicity against SCLC, none of the simple BK antagonists were toxic to cells, although they were very effective for inhibition of BK-evoked elevation of intracellular free calcium in SCLC cultures. Typical of this behavior is B-9430, a very potent 'third-generation' BK antagonist which is active against both B1 and B2 BK receptors and shows a long half-life in vivo. When this antagonist was **crosslinked** by suberimide at the N-terminus (B-201), potent cytoxic activity was found. Dimers of 'first-generation' BK antagonists, such as CP-127, were introduced by investigators at Cortech , and while they are quite potent antagonists in many BK assays, were not cytotoxic. When the **linker** in CP-127 was moved to the N-terminus of the dimer (B-197) significant toxicity was found. Even dimers of the potent 'second-generation' Hoechst antagonist HOE-140 showed only low cytotoxicity against SCLC. Orosz et al. reported that a pseudopeptide substance P antagonist (B-237) was active against SCLC. The authors confirmed this activity, and found that neither a homodimer (B-240) nor a heterodimer of this peptide with the best BK antagonist (B-215) showed increased cytotoxicity. Certain of these new dimers are toxic to SCLC lines that show multidrug resistance phenotypes, testifying to the different mechanism of toxicity of these agents. Preliminary studies indicate that these new dimers act by stimulation of apoptosis in

SCLC cells. Peptide dimer B-201 inhibited the growth of SCLC cell line SHP-77 when implanted s.c. in athymic (nude) mice. These dimers offer a new avenue for anti-cancer drug development.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:514959 HCAPLUS
DOCUMENT NUMBER: 131:299676
TITLE: Thermodynamic melting studies on oligonucleotide-peptide **conjugates**
AUTHOR(S): Frier, C.; Harrison, J. G.; Balasubramanian, S.
CORPORATE SOURCE: Department of Chemistry, Cambridge University, Cambridge, CB2 1EW, UK
SOURCE: Nucleosides & Nucleotides (1999), 18(6 & 7), 1477-1478
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A symposium report. A small library of oligonucleotide-peptide **conjugates** has been prepd. and studied to explore the influence of the various peptide side chain (cationic, anionic or hydrophobic) on the hybridization properties of the DNA.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:450816 HCAPLUS
DOCUMENT NUMBER: 131:113237
TITLE: Technetium-99m labeled peptides for thrombus imaging
INVENTOR(S): Dean, Richard T.; Lister-James, John
PATENT ASSIGNEE(S): Diatide, Inc., USA
SOURCE: U.S., 43 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 44
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5925331	A	19990720	US 1995-335832	19950105
WO 9323085	A1	19931125	WO 1993-US4794	19930521
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1004322	A2	20000531	EP 1999-124003	19930521
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
US 5997845	A	19991207	US 1997-902367	19970729
JP 10291939	A2	19981104	JP 1998-45661	19980226
JP 3380738	B2	20030224		

PRIORITY APPLN. INFO.:

US 1992-886752	B2	19920521
WO 1993-US4794	W	19930521
US 1991-653012	B2	19910208
US 1992-893981	A3	19920605
US 1993-44825	B1	19930408
EP 1993-914023	A3	19930521
JP 1994-503844	A3	19930521
US 1994-273274	A2	19940711
US 1995-439905	A3	19950512
US 1995-462668	B1	19950605

US 1995-469858 A 19950606

AB Radiolabeled reagents are provided that are scintigraphic imaging agents for imaging sites of thrombus formation in vivo, as are methods for producing such reagents. Specifically, the invention relates to reagents each comprised of a specific binding compd., capable of binding to at least one component of a thrombus, covalently **linked** to a radiolabel-binding moiety. The invention provides these reagents, methods and kits for making such reagents, and methods for using such reagents labeled with technetium-99m to image thrombus sites in a mammalian body.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:220014 HCAPLUS
DOCUMENT NUMBER: 130:249137
TITLE: Novel targeted ultrasound imaging contrast agents for diagnostic and therapeutic use
INVENTOR(S): Unger, Evan C.; Fritz, Thomas A.; Gertz, Edward W.
PATENT ASSIGNEE(S): ImarRx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913919	A1	19990325	WO 1998-US18858	19980909
W: AU, CA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6139819	A	20001031	US 1997-932273	19970917
AU 9893830	A1	19990405	AU 1998-93830	19980909
EP 959908	A1	19991201	EP 1998-946919	19980909
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.:
US 1997-932273 A 19970917
US 1995-497684 B2 19950607
US 1996-640464 B2 19960501
US 1996-660032 B2 19960606
US 1996-666129 A2 19960619
WO 1998-US18858 W 19980909

AB This invention describes novel contrast agents which may be used for diagnostic and therapeutic use. The compns. may comprise a lipid, a protein, polymer and/or surfactant, and a gas, in combination with a targeting ligand. In preferred embodiments, the targeting ligand targets coagula, including emboli and/or thrombi, particularly in patients suffering from an arrhythmic disorder. The contrast media can be used in conjunction with diagnostic imaging, such as ultrasound, as well as therapeutic applications, such as therapeutic ultrasound.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

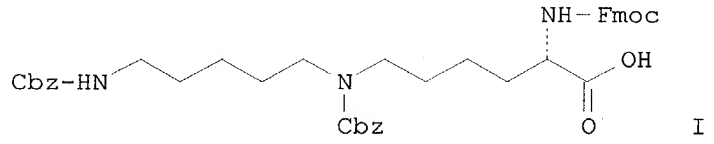
L18 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:796149 HCAPLUS
DOCUMENT NUMBER: 130:205609
TITLE: Coupling of Nuclear Localization Signals to Plasmid DNA and Specific Interaction of the **Conjugates** with Importin .alpha.
AUTHOR(S): Ciolina, Carole; Byk, Gerardo; Blanche, Francis;

Thuillier, Vincent; Scherman, Daniel; Wils, Pierre
CORPORATE SOURCE: Centre de Recherche de Vitry Alfortville, UMR 133 CNRS/Rhone-Poulenc Rorer and Rhone-Poulenc Rorer Gencell, Vitry-sur-Seine, 94403, Fr.
SOURCE: Bioconjugate Chemistry (1999), 10(1), 49-55
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nuclear localization signal (NLS) of the SV40 large T antigen efficiently induces nuclear targeting of proteins. We have developed a chem. strategy for covalent coupling of NLS peptides to plasmid DNA. A p-azido-tetrafluoro-benzyl-NLS peptide **conjugate** was synthesized. This **conjugate** was used to covalently assoc. NLS peptides to plasmid DNA by photoactivation. Reporter gene was expressed after transfection of the plasmid-NLS **conjugates** in NIH 3T3 cells. The **conjugates** interacted specifically with the NLS-receptor importin .alpha., but plasmid-NLS **conjugates** were not detected in the nucleus, by fluorescence microscopy, after cytoplasmic microinjection.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:683624 HCAPLUS
DOCUMENT NUMBER: 130:92190
TITLE: Polylysine-Gd-DTPAn and polylysine-Gd-DOTAn coupled to anti-CEA F(ab')2 fragments as potential immunocontrast agents: relaxometry, biodistribution, and magnetic resonance imaging in nude mice grafted with human colorectal carcinoma
AUTHOR(S): Curtet, Chantal; Maton, Frederic; Havet, Thierry; Slinkin, Micha; Mishra, Anil; Chatal, Jean-Francois; Muller, Robert N.
CORPORATE SOURCE: Laboratoire de Biophysique, INSERM Unite de Recherche, Institut de Biologie, Nantes, F44035, Fr.
SOURCE: Investigative Radiology (1998), 33(10), 752-761
CODEN: INVRAV; ISSN: 0020-9996
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunocontrast agents used for magnetic resonance imaging require antibodies that preserve the immunoreactivity while contg. a high no. of chelated paramagnetic ions. Anti-CEA F(ab')2 fragments were coupled to polylysine-Gd-DOTA and polylysine-Gd-DTPA. A paramagnetic load as high as n = 24 to 28 metal ions per antibody was reached. The immunoreactivity of the gadolinium (Gd)-labeled anti-CEA F(ab')2 **immunoconjugates** was 80% to 85%. Compared with that of com. chelates, the relaxivity (R1) increase is as follows: Gd-DTPA < Gd-DOTA < Gd-H2O < PL-Gd-DTPA24-28 < PL-Gd-DTPA24-28 F(ab')2 < PL-Gd-DOTA24-28 < PL-Gd-DOTA24-28 F(ab')2. 1H nuclear magnetic relaxation dispersion data of **immunoconjugates** showed that the high relaxivity enhancement was the result of a redn. of the mol. tumbling rate. Twenty-four hours after i.v. injection of 50 .mu.g (1 .mu.mol Gd/kg) of Gd-labeled **immunoconjugates** to nude mice grafted with human colorectal carcinoma LS 174T, the tumor uptake was 10% to 15%, resulting in an increase of R1 of up to 15% to 20% vs. noninjected mice. No difference was found between PL-Gd-DTPA24-28 F(ab')2 and PL-Gd-DOTA24-28 F(ab')2 **immunoconjugates** for tumor, liver, and kidney uptake. A high signal intensity of tumor was obsd. in 50% of the tested mice.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:549007 HCAPLUS
DOCUMENT NUMBER: 129:276305
TITLE: Synthesis of Reagents for the Construction of Hypusine and Deoxyhypusine Peptides and Their Application as Peptidic Antigens
AUTHOR(S): Bergeron, Raymond J.; Weimar, William R.; Mueller, Ralf; Zimmerman, Curt O.; McCosar, Bruce H.; Yao, Hua; Smith, Richard E.
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610-0485, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(20), 3888-3900
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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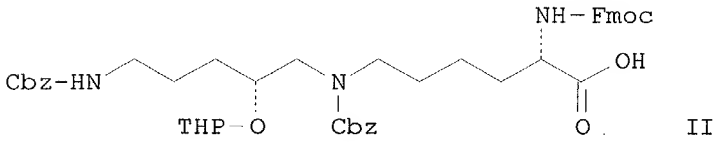

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AB Two new synthetic methods which allow access to (2S)-deoxyhypusine, natural (2S,9R)-hypusine, (2S,9S)-hypusine, and deoxyhypusine- and hypusine-contg. peptides are described. Hypusine [Hpu] is (2S,9R)-2,11-diamino-9-hydroxy-7-azaundecanoic acid. The methods involve both the construction of a deoxyhypusine reagent I in which the .alpha.-nitrogen protecting group is orthogonal to the N-7 and N-12 protecting groups and an alternate synthesis of our previous hypusine reagent II, a synthesis which provides for better stereochem. control at C-9. Synthetic hypusine and deoxyhypusine can be generated from these reagents. The hypusine-contg. hexapeptide (Cys-Thr-Gly-Hpu-His-Gly) is **conjugated** to ovalbumin (OVA), keyhole limpet hemocyanin (KLH), and a bis-maleimide; KLH **conjugates** are also made with the deoxyhypusine- and lysine-contg. hexapeptides. Monoclonal antibodies are generated to the hypusine-contg. hexapeptide-OVA **conjugate** in mice. These are isolated and screened against the hypusine-contg. hexapeptide-KLH and hypusine-contg. hexapeptide-bis-maleimide **conjugates**, as well as against the deoxyhypusine-contg. and lysine-contg. hexapeptide-KLH **conjugates**. These antibodies may be useful in localizing intracellular hypusine-contg. peptides as well as

peptides contg. hypusine analogs.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:464791 HCAPLUS
DOCUMENT NUMBER: 129:260801
TITLE: Synthesis and hybridization analysis of a small library of peptide oligonucleotide **conjugates**
AUTHOR(S): Harrison, Joseph G.; Balasubramanian, Shankar
CORPORATE SOURCE: University Chemical Laboratory, Cambridge University, Cambridge, CB2 1 EW, UK
SOURCE: Nucleic Acids Research (1998), 26(13), 3136-3145
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A small library of 49 peptide-oligonucleotide **conjugates** were synthesized to explore the influence of various peptide side chains on the hybridization properties of the DNA. An invariant 8mer oligonucleotide was coupled to a peptide portion that contained a five residue variable region composed of the cationic amino acids lysine, ornithine, histidine and arginine, the hydrophobic amino acid tryptophan, and alanine as a spacer. Melting temp. anal. indicated that Tm depended principally on the no. of cationic residues. The free energies of binding for polycationic peptide-oligonucleotides were enhanced compared with the unmodified 8mer. The origin of this stabilizing effect was found to be derived from a more exothermic enthalpic term. Improvement in .DELTA.GvH was found to depend on the presence of pos. charge and also the exact identity of the cationic amino acid, with the polyarginine peptide giving the most favorable .DELTA.GvH value and the most exothermic .DELTA.HvH. Further exploration suggested that the cationic peptide fragments interacted mainly with single-stranded rather than duplex DNA. A study of pH dependence showed that the polyhistidine **conjugate** was particularly sensitive to pH changes near neutrality, as indicated by a significant rise in Tm from 19.5.degree. at pH 8.0 to 28.5.degree. at pH 6.0.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:243945 HCAPLUS
DOCUMENT NUMBER: 129:19607
TITLE: Three-dimensional extracellular matrix engineering in the nervous system
AUTHOR(S): Borkenhagen, M.; Clemence, J.-F.; Sigrist, H.; Aebischer, P.
CORPORATE SOURCE: Division of Surgical Research and Gene Therapy Center, Cent. Hospitalier Universitaire Vaudois, Lausanne University Medical School, Lausanne, 1011, Switz.
SOURCE: Journal of Biomedical Materials Research (1998), 40(3), 392-400
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Growing neurites are guided through their environment during development and regeneration via different cellular and extracellular matrix (ECM) mol. cues. To mimic cell-matrix interactions, a three-dimensional (3D) hydrogel-based ECM equiv. contg. a covalently i.m.- mobilized laminin oligopeptide sequence was designed to facilitate nerve regeneration. This

study illustrates that the oligopeptide domain CDPGYIGSR covalently **linked** to an agarose gel as a bioartificial 3D substrate successfully supports neurite outgrowth from dorsal root ganglia (DRG) in vitro. The specificity of the neurite promoting activity was illustrated through the inhibition of neurite outgrowth from DRG in a CDPGYIGSR-derivatized gel in the presence of solubilized CDPGYIGSR peptide. Gels derivatized with CDPGYIGSK and CDPGRGSYI peptides stimulated a smaller increase of neurite outgrowth. In vivo expts. revealed the capability of a CDPGYIGSR-derivatized gel to enhance nerve regeneration in a transected rat dorsal root model compared to an underivatized gel, a CDPGRGSYI gel, and saline-filled nerve guidance channels. These data suggest the feasibility of a 3D hydrogel-based ECM equiv. capable of enhancing neurite outgrowth in vitro and in vivo.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:219310 HCAPLUS
DOCUMENT NUMBER: 128:253795
TITLE: Use of biologically active peptides to increase the efficiency of transformation with DNA:cationic lipid complexes
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.
PATENT ASSIGNEE(S): Life Technologies, Inc., USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 447,354, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5736392	A	19980407	US 1996-658130	19960604
US 6051429	A	20000418	US 1997-818200	19970314
US 2003144230	A1	20030731	US 2002-200879	20020723

PRIORITY APPLN. INFO.: US 1995-477354 B2 19950607
US 1996-658130 A2 19960604
US 1997-818200 A2 19970314
US 1998-39780 A1 19980316
US 2001-911569 A1 20010723

AB Biol. active peptides, such as receptor ligands, fusogenic peptides, or nuclear localization signals are incorporated into complexes of DNA and cationic lipids to increase the effectiveness of transformation of eukaryotic cells. These peptides may also be **conjugated** with a DNA-binding peptide or group such as spermine. Methods for the prepn. of transfecting compns. and use as intracellular delivery agents and extracellular targeting agents are also disclosed. Transformation efficiencies of animal cell lines with LipofectAMINE.RTM. liposomes were increased by up to .apprx.50-fold when **conjugates** of viral RGD peptides and spermine were added to the complex.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:317762 HCAPLUS
DOCUMENT NUMBER: 126:288568
TITLE: Cytolytic dimers of bradykinin antagonists and

neurokinin receptor antagonists
INVENTOR(S): Whalley, Eric T.; Stewart, John M.; Chan, Daniel C.; Gera, Lajos
PATENT ASSIGNEE(S): Cortech, Inc., USA; University Technology Corporation
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709347	A1	19970313	WO 1996-US14113	19960903
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5849863	A	19981215	US 1995-526065	19950908
CA 2230907	AA	19970313	CA 1996-2230907	19960903
AU 9669119	A1	19970327	AU 1996-69119	19960903
EP 848718	A1	19980624	EP 1996-929871	19960903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1995-526065 19950908
WO 1996-US14113 19960903

AB The present invention provides bradykinin antagonist dimers (BKA1-X-BKA2 wherein BKA1 and BKA2 are bradykinin antagonists and X is a **linker** group) capable of inhibiting cancer cell growth; BKA2 is optionally absent. The anticancer agents can also be compds. comprising a bradykinin antagonist and a neurokinin receptor antagonist with the general formula BKA-X-Y, where BKA is a bradykinin antagonist, X is a **linker**, and Y is a neurokinin receptor antagonist. Addnl., the compds. of the invention can by dimerized neurokinin receptor antagonists (Y1-X-Y2). Methods are also provided for inhibiting lung cancer cell growth by administering a therapeutically effective amt. of one or more of the above compds.

L18 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:204391 HCAPLUS
DOCUMENT NUMBER: 126:264360
TITLE: Preparation of heterodimeric peptides as bradykinin receptor antagonists with neurokinin receptor blocking activity
INVENTOR(S): Goodfellow, Val S.; Whalley, Eric T.; Wincott, Francine E.
PATENT ASSIGNEE(S): Cortech, Inc., USA
SOURCE: U.S., 13 pp., Cont\.-in-part of U.S. Ser.No. 974,000, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5610140	A	19970311	US 1994-284068		19940801
US 5416191	A	19950516	US 1993-2684		19930108
US 5635593	A	19970603	US 1995-440352		19950512
PRIORITY APPLN. INFO.:			US 1991-677391	B2	19910401
			US 1992-859582	B2	19920327
			US 1992-974000	B2	19921110
			US 1994-227184	A1	19940413

OTHER SOURCE(S): MARPAT 126:264360
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides heterodimeric compds. Z1-Z0-A1-B2-C3-D4-E5-F6(X)-G7-H8-I9-J10 [Z1 = absent, H, Ac, adamantylacetyl, C1-8-alkyl, -alkanoyl, arylsulfonyl, alkoxycarbonyl, dihydroquinuclidinylcarbonyl; Z0 = absent, D-Arg, L-Arg, D-Lys, L-Lys, D-Orn, L-Orn, H2NC(:NH)NH(CH2)nCO, n = 3-6, Arg substitute; A1 = D-Arg, L-Arg, D-Lys, L-Lys, D--Orn, L-Orn, Arg substitute; B2 = Pro, Hyp, Gly, Ser, Thr, N-MeSer, N-MeThr, NR1CHR2CO, R1, R2 = independently H, alkyl, aryl, heteroaryl, alkylamino; D4 = Gly, Ala, thienylalanine; E5 = (un)substituted Phe, Gly, cyclopentylglycine, cyclohexylglycine, cyclohexylalanine, 2-indanylglycine, 2-thienylalanine, N-substituted Gly; F6 = Cys, homocysteine, penicillamine, .beta.-methylcysteine, thiol-contg. amino acid; G7 = arom. amino acid; H8 = amino acid; I9 = OH or basic, acidic, or neutral amino acid; J10 = absent, OH; X = Q1, Q2; Z = succinimido, Ph, pyrrolidinone where S atom of F6 is attached; m = 1-8; A = amino acid; L = arom. amino acid; R3 = Me, lower alkyl; R4 = (un)substituted benzyl, phenethyl, lower alkyl, indolylethyl; R5 = H, Me, CHO, Ac, lower alkyl, substituted carboxyl; R = N, CH; Q = NH, NR5] possessing bradykinin and neurokinin receptor antagonist activities useful in the treatment of asthma and other inflammatory diseases esp. those involving the airway or pulmonary system. The present invention is also useful in the treatment of pain and inflammation. Thus, treatment of 73 mg neurokinin-1 (NK1) receptor antagonist CP-0126 tetratrifluoroacetate salt (H-D-Arg-Arg-Pro-Hyp-Gly-Phe-Cys-D-Phe-Leu-Arg-OH.4CF3CO2H) with 32 mg maleiminohexanoyl peptide I [Nal = 3-(2-naphthyl)-L-alanine] (prepn. given) in DMF-aq. ammonium bicarbonate gave 50 mg heterodimeric peptide II. In vitro studies of II in human plasma, guinea pig plasma, rat kidney, and pig kidney showed half-life stabilities all >6 h. II inhibited both bradykinin- and substance P Me ester-induced increases in guinea pig lung resistance (indicative of airway constriction) with ED50 = 30 .mu.mg/kg/min and 2 .upsilon.g/kg/min, resp.

L18 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:130043 HCAPLUS
DOCUMENT NUMBER: 126:127859
TITLE: Use of biologically active peptides to increase the efficiency of transformation with DNA:cationic lipid complexes
INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.
PATENT ASSIGNEE(S): Life Technologies, Inc., USA; Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640961	A1	19961219	WO 1996-US8723	19960604
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9659792	A1	19961230	AU 1996-59792	19960604
EP 874910	A1	19981104	EP 1996-917118	19960604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
JP 11506935	T2	19990622	JP 1996-501227	19960604

PRIORITY APPLN. INFO.: US 1995-477354 A 19950607
WO 1996-US8723 W 19960604

AB Biol. active peptides, such as receptor ligands, fusogenic peptides, or nuclear localization signals are incorporated into complexes of DNA and cationic lipids to increase the effectiveness of transformation of eukaryotic cells. These peptides may also be **conjugated** with a DNA-binding peptide or group such as spermine. Methods for the prepn. of transfecting compns. and use as intracellular delivery agents and extracellular targeting agents are also disclosed. Transformation efficiencies of animal cell lines with LipofectAMINE.RTM. liposomes were increased by up to .apprx.50-fold when **conjugates** of viral RGD peptides and spermine were added to the complex.

L18 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:107372 HCAPLUS
DOCUMENT NUMBER: 126:115164
TITLE: Sequestered imaging agents for high-resolution diagnostic imaging, and preparation thereof
INVENTOR(S): Pollak, Alfred
PATENT ASSIGNEE(S): Resolution Pharmaceuticals Inc., Can.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9638185	A1	19961205	WO 1996-CA310	19960516
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5804158	A	19980908	US 1995-454859	19950531
CA 2218877	AA	19961205	CA 1996-2218877	19960516
AU 9656818	A1	19961218	AU 1996-56818	19960516
AU 699383	B2	19981203		
EP 828521	A1	19980318	EP 1996-914809	19960516
EP 828521	B1	20020828		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
JP 11505852 T2 19990525 JP 1996-536048 19960516
AT 222777 E 20020915 AT 1996-914809 19960516
PRIORITY APPLN. INFO.: US 1995-454859 A 19950531
WO 1996-CA310 W 19960516

AB Compds. useful for high resoln. diagnostic imaging incorporate an imaging agent having a chelator that is **linked** by a metal-cleavable bond to a ligand that has affinity for a site removed from the site of diagnostic interest. Upon labeling, the ligand is cleaved leaving the labeled imaging agent free to localize at the site of diagnostic interest unhindered, while the ligand and nay unlabeled imaging agent is sequestered to the removed site. By sequestering unlabeled imaging agent, the labeled imaging agent does not compete to occupy the site of interest, resulting in images of enhanced resoln.

L18 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:639667 HCAPLUS
DOCUMENT NUMBER: 125:298979
TITLE: Synthesis of chimeric BR96 peptide-dox **conjugates** and their binding specificity toward 1C2/10 antibody
AUTHOR(S): Wu, Y.; Palmoski, M.; Kirkley, D.; Root, B.; Knupp, C.; Cash, P.; Wents, E.; Dodsworth, D.; Alexander, A.; et al.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Syracuse, NY, 13221, USA
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995) , Meeting Date 1994, 867-868. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Four chimeric BR96 peptide-dox **conjugates** were prepd. for detection of monoclonal antibody 1C2/10. Monoclonal antibody 1C2/10 is a monoclonal antibody generated as a specific reagent to detect antibody BR96-doxorubicin **conjugates** that targets Lewis Y antigen and kill tumor cells.

L18 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:407987 HCAPLUS
DOCUMENT NUMBER: 125:186503
TITLE: Novel bradykinin antagonist dimers for the treatment of human lung cancers
AUTHOR(S): Chan, Daniel; Gera, Lajos; Helfrich, Barbara; Helm, Karen; Stewart, John; Whalley, Eric; Bunn, Paul
CORPORATE SOURCE: Department of Medicine, University of Colorado Cancer Center, Denver, CO, 80262, USA
SOURCE: Immunopharmacology (1996), 33(1-3, Papers presented at KININ '95, Fourteenth International Symposium on Bradykinin and Related Kinins, 1995), 201-204
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Evidence is presented that a novel class of bradykinin antagonist dimers, synthesized by **crosslinking** the third generation bradykinin antagonist with appropriate **crosslinkers**, have increased potency and plasma stability. Several of these antagonists are able to selectively inhibit the growth of small cell lung cancer cells at

.ltoreq.10 .mu.M. These new bradykinin antagonists dimers may have clin. pot. for the prevention and(or) treatment of human lung cancers.

L18 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:407963 HCAPLUS
DOCUMENT NUMBER: 125:186044
TITLE: A new class of potent bradykinin antagonist dimers
AUTHOR(S): Gera, Lajos; Stewart, John M.; Whalley, Eric; Burkard, Michael; Zuzack, John S.
CORPORATE SOURCE: Department of Biochemistry, University of Colorado School of Medicine, Denver, CO, 80262, USA
SOURCE: Immunopharmacology (1996), 33(1-3, Papers presented at KININ '95, Fourteenth International Symposium on Bradykinin and Related Kinins, 1995), 178-182
CODEN: IMMUDP; ISSN: 0162-3109
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors report here dimers of their potent new bradykinin antagonists (such as B 9430) that contain .alpha.-(2-indanyl)glycine and have both B1 and B2 receptor antagonist activity. In these new dimers, the **crosslinkers** are generally at the N-terminus of the peptide chain. The authors have synthesized dimers having succinyl-, suberyl-, suberimidyl- and bis-succinimidohexane **linkers**. Many of these dimers show high affinities for human and guinea pig B1 and B2 receptors.

L18 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:348017 HCAPLUS
DOCUMENT NUMBER: 125:96258
TITLE: Analysis of monoclonal antibody and **immunoconjugate** digests by capillary electrophoresis and capillary liquid chromatography
AUTHOR(S): Liu, Jinping; Zhao, Huiru; Volk, Kevin J.; Klohr, Steven E.; Kerns, Edward H.; Lee, Mike S.
CORPORATE SOURCE: Analytical Research and Development, Bristol-Myers Squibb Pharmaceutical Research Institute, 5 Research Parkway, Wallingford, CT, 06492, USA
SOURCE: Journal of Chromatography, A (1996), 735(1 + 2), 357-366
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Comparative peptide mapping of a monoclonal antibody chimeric BR96 and corresponding doxorubicin (DOX) **immunoconjugate** was performed using capillary electrophoresis (CE) and capillary liq. chromatog. (CLC). A unique, highly sensitive and selective approach combined with both UV absorbance and laser-induced fluorescence (LIF) detection has been developed and applied to studies including enzymic digests of antibody and **conjugate** and related drug and **conjugation linker** substances. The anal. methodol. has been established based on the unique characteristic of the anticancer drug DOX which yields native fluorescence. With an excitation wavelength of 488 nm from argon-ion laser, DOX **conjugated** to the monoclonal antibody using a hydrazone **linker** can be detd. with a detection limit at the attomole level. Approaches were developed based on the successful **conjugation** and anal. of a model peptide **conjugate**. Enzymic digests of the monoclonal antibody BR96 and its **immunoconjugate** were mapped by CE and CLC with online UV and LIF detection, which results in a unique fingerprint for structural anal.

With a two-dimensional LC-CE approach, **conjugated** peptide-DOX species from LC were further analyzed by CE with LIF detection. The drug-contg. peptide fragments in the mixt. were readily detected, which can be further characterized using other complementary anal. techniques.

L18 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:207221 HCAPLUS
DOCUMENT NUMBER: 124:344082
TITLE: Synthesis, secondary structure and folding of the bend region of lung surfactant protein B
AUTHOR(S): Waring, A. J.; Faull, K. F.; Leung, C.; Chang-Chien, A.; Mercado, P.; Taeusch, H. W.; Gordon, L. M.
CORPORATE SOURCE: Dep. Psychistry, Drew Univ., Los Angeles, CA, USA
SOURCE: Peptide Research (1996), 9(1), 28-39
CODEN: PEREEO; ISSN: 1040-5704
PUBLISHER: Eaton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous theor. anal. of the primary structure of lung surfactant protein SP-B indicates a disulfide-**linked**, hydrophobic mid-sequence that forms a hairpin-like motif. Here, the authors exptl. investigate the secondary structure of the disulfide-stabilized bend region by synthesizing two 12-residue analogs of the SP-B midsequence. The native peptide has the same sequence for residues 35-46 as native human SP-B, while, in the second mimic peptide, Leu40 and Val41 were replaced with D-Ser and L-His. Both peptides contain cysteine residues at the N- and C-terminus (Cys35 and Cys46, resp.). Oxidn.-redn. expts. with fast atom bombardment mass spectroscopy showed mass shifts of approx. 2 daltons, consistent with the oxidized peptides existing in soln. as monomers, each with one internal disulfide bond (Cys35-Cys46). Since CD and Fourier-transform IR measurements show that both peptides assume turn conformations in structure-promoting solvents such as trifluoroethanol (TFE), a structural model is proposed in which Cys35 and Cys46 are brought in close apposition through an internal bend in the peptide. Consistent with this model are ESR results of the mimic peptide in TFE, ESR spectra indicated broadening characteristic of either radical interactions or decreased mobility, or both. Increases in radical interactions for the double spin-labeled mimic peptide would be expected for Cys35 and Cys46 approaching within 14 .ANG. in structure-promoting solvents, while decreases in spin-label mobility could be due to the formation of a loop. Based on these observations with peptide analogs, residues 35-46 probably form a similar bend in the full-length protein.

L18 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:750498 HCAPLUS
DOCUMENT NUMBER: 123:170076
TITLE: Preparation of cobalamin **conjugates** for determination of vitamin B12.
INVENTOR(S): Hoess, Eva; Stock, Werner; Huber, Erasmus
PATENT ASSIGNEE(S): Boehringer Mannheim GmbH, Germany
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 599325	A1	19940601	EP 1993-119041	19931125

EP 599325 B1 19990303
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE
DE 4239815 A1 19940601 DE 1992-4239815 19921126
AT 177110 E 19990315 AT 1993-119041 19931125
PRIORITY APPLN. INFO.: DE 1992-4239815 19921126
OTHER SOURCE(S): MARPAT 123:170076
AB BCOSpP (B = cobalamin minus a CONH2 group; P = coupling partner; Sp = spacer group), were prepd. from BCO2H and ClCO2R2 via a BCO2CO2R2 intermediate (R2 = alkyl). Thus, vitamin B12 d-acid in DMF/DMSO was treated with Et3N, iso-Bu chloroformate, and H2NCH2CH2OCH2CH2OCH2CH2NHCOCH 2CH2SAc.CF3CO2H [DADOO-(S)ATP] (prepn. given) to give 25% B12-d-DADOO-(S)ATP. This was activated with aq. hydroxylamine and coupled with prepolymd. peroxidase (pPOD) activated with maleimidohexanoyl-N-hydroxysuccinimide ester (MHS) to give a B12-d-DADOO-S-pPOD with superior properties for vitamin B12 detn. using monoclonal antibodies.

L18 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:666978 HCAPLUS
DOCUMENT NUMBER: 123:51500
TITLE: Photoimmobilization of a Bioactive Laminin Fragment and Pattern-Guided Selective Neuronal Cell Attachment
AUTHOR(S): Clemence, Jean-Francois; Ranieri, John P.; Aebischer, Patrick; Sigrist, Hans
CORPORATE SOURCE: Institute of Biochemistry, University of Berne, Bern, CH-3012, Switz.
SOURCE: Bioconjugate Chemistry (1995), 6(4), 411-17
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To attain light-dependent functionalization of biocompatible materials, a photolabel-derivatized, bioactive laminin fragment has been synthesized, chem. characterized, and photoimmobilized. Covalent high-resoln. patterning of the laminin fragment CDPGYIGSR to hydroxylated fluorinated ethylene propylene (FEP-OH), poly(vinyl alc.), and glycophase glass has been achieved. The synthetic peptide CDPGYIGSR was thermochem. coupled to either N-[m-[3-(trifluoromethyl)diazirin-3-yl]phenyl]-4-maleimidobutyramide or 4-maleimidobenzophenone. Photolabel-derivatized peptides were radiolabeled, and 20 and 300 .mu.m-sized patterns were visualized by autoradiog. The biospecific interaction of photoimmobilized laminin fragments with cells was investigated by analyzing the selective attachment of NG 105-15 neuroblastoma .times. glioma cells which bear CDPGYIGSR-specific cell surface receptors. On photopatterned FEP-OH membranes NG 108-15 cells differentiated in serum-supplemented media within 1 day. Specific attachment to the immobilized oligopeptide CDPGYIGSR was assessed in serum-free media with competitive binding studies, showing an 82% decrease in cell adherence after the cell receptors were blocked with sol. CDPGYIGSR.

L18 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:549076 HCAPLUS
DOCUMENT NUMBER: 121:149076
TITLE: Preparation of bradykinin antagonists with **conjugated** pharmacophores for treatment of inflammation or pain
INVENTOR(S): Chronis, John C.; Blodgett, James K.; Goodfellow, Val Smith; Marathe, Manoj V.; Spruce, Lyle W.; Whalley, Eric T.
PATENT ASSIGNEE(S): Cortech, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9411021	A1	19940526	WO 1993-US10222	19931029
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9308014	A	19940711	ZA 1993-8014	19931027
CA 2147869	AA	19940526	CA 1993-2147869	19931029
AU 9454109	A1	19940608	AU 1994-54109	19931029
EP 671941	A1	19950920	EP 1993-924412	19931029
R: CH, DE, ES, FR, GB, IT, LI, SE				
JP 08503460	T2	19960416	JP 1993-512112	19931029
CN 1094058	A	19941026	CN 1993-114484	19931110

PRIORITY APPLN. INFO.: US 1992-974000 A 19921110
WO 1993-US10222 W 19931029

AB A heterodimeric bradykinin antagonist is disclosed of formula (BKAn)(X)(Y), where BKAn is a bradykinin antagonist peptide, Y is a pharmacophore, and X is a bridging **linker** chem. joining BKAn and Y components. The Y pharmacophore moiety may be e.g. a .mu.-opioid receptor agonist, a neutrophil elastase inhibitor, or a cyclooxygenase inhibitor. These antagonists are dual-action compds. which can interact with 2 receptor populations or with a receptor and an enzyme. The bradykinin antagonists of the invention are useful for treating pain or inflammation. Prepn. of the bradykinin antagonists is included.

L18 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:239252 HCAPLUS
DOCUMENT NUMBER: 120:239252
TITLE: Technetium-99m labeled peptides for imaging
INVENTOR(S): Dean, Richard T.; Lister-James, John
PATENT ASSIGNEE(S): Diatech, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 44
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325244	A1	19931223	WO 1993-US5372	19930604
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5508020	A	19960416	US 1992-893981	19920605
AU 9345287	A1	19940104	AU 1993-45287	19930604
AU 688264	B2	19980312		
EP 644778	A1	19950329	EP 1993-915221	19930604
EP 644778	B1	19970514		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
AT 152918	E	19970515	AT 1993-915221	19930604
ES 2105292	T3	19971016	ES 1993-915221	19930604
JP 2954354	B2	19990927	JP 1993-501622	19930604

CA 2137009	C	20011127	CA 1993-2137009	19930604
US 5951964	A	19990914	US 1995-341537	19950126
US 5976494	A	19991102	US 1995-469858	19950606
US 6113878	A	20000905	US 1995-467567	19950606
US 5997845	A	19991207	US 1997-902367	19970729

PRIORITY APPLN. INFO.:
US 1992-893981 A2 19920605
US 1991-653012 B2 19910208
US 1992-886752 B1 19920521
US 1993-44825 B1 19930408
WO 1993-US5372 A 19930604
US 1994-273274 A2 19940711
US 1995-439905 A3 19950512
US 1995-462668 B1 19950605
US 1995-469858 A 19950606

OTHER SOURCE(S): MARPAT 120:239252

AB Radiolabeled reagents, esp. peptides with specific binding properties, and their prepn. for use as scintigraphic imaging agents are described. Reagents, methods and kits for making labeled peptides, and methods for using them labeled with technetium-99m (Tc-99m) via Tc-99m binding moieties comprising said reagents, are described. In particular, the specific-binding peptides and Tc-99m binding moieties of these reagents are covalently **linked** to a polyvalent **linker** that is covalently **linked** to several of the specific-binding peptides, and the Tc-99m binding moieties are covalently **linked** to several of the specific-binding peptides, the polyvalent **linker** moiety, or to both the specific-binding peptides and the polyvalent **linker** moiety. The Tc chelating moiety BAT-BM (N-[N',N'-bis(2-maleimidoethyl)aminoethyl)]-N6,N9-bis(2-methyl-2-triphenylmethylthiopropyl)-6,9-diazanonanamide was prepd. by the reaction of N9-(t-butoxycarbonyl)-N6,N9-bis(2-methyl-2-triphenylmethylthiopropyl)-6,9-diazanonanoic acid with N-hydroxy succinimide and tris-(2-aminoethyl)amine. The polyvalent **linking** moiety TMEA, tris(2-maleimidoethyl)amine, was synthesized by the reaction of tris(2-aminoethyl)amine and N-carbomethoxymaleimide. Peptides for the reagents were prepd. by Fmoc chem. and **conjugated** with the **linking** moiety and the chelating moieties through reactive groups on the peptide. The use of one such peptide in the imaging of deep vein thrombosis of dogs is demonstrated.

L18 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:186773 HCAPLUS
DOCUMENT NUMBER: 120:186773
TITLE: Engineered protein chelates suitable for fluorescent lanthanide-based time resolved fluorescence assays
INVENTOR(S): Banville, Dennis; Macmanus, John P.; Marsden, Brian; Szabo, Arthur G.; Hogue, Christopher; Sikorska, Marianna
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 77 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2082770	AA	19930826	CA 1992-2082770	19921112

PRIORITY APPLN. INFO.: US 1992-841657 19920225
OTHER SOURCE(S): MARPAT 120:186773

AB Chelator sequences of 12 amino acids can form complexes with luminescent lanthanides, e.g. Tb and Eu. The complexes display high affinity between chelator and lanthanide and are useful as probes in fluorescent (immuno)assays. Oncomodulin was modified by cassette mutagenesis to replace the naturally occurring CD loop by the sequence Asp-Lys-Asn-Ala-Asp-Gly-Cys-Ile-Glu-Phe-Glu-Glu and the naturally occurring Cys at position 18 was removed by site-specific mutagenesis and replaced by Val. The chromophore 7-diethylamino-3-((4'-iodoacetylamino)phenyl)-4-methylcoumarin was covalently bonded to the Cys in the recombinant protein. Eu3+ was added to the modified oncomodulin and luminescence was measured.

L18 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:184644 HCAPLUS
DOCUMENT NUMBER: 120:184644
TITLE: Self-assembling polynucleotide delivery system for genetic transformation and gene therapy
INVENTOR(S): Szoka, Francis C., Jr.; Haensler, Jean
PATENT ASSIGNEE(S): University of California, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9319768	A1	19931014	WO 1993-US3406	19930405
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9340278	A1	19931108	AU 1993-40278	19930405
AU 682308	B2	19971002		
EP 636028	A1	19950201	EP 1993-909508	19930405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07505639	T2	19950622	JP 1993-517793	19930405
EP 1236473	A2	20020904	EP 2002-1408	19930405
EP 1236473	A3	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6300317	B1	20011009	US 1995-469899	19950606
US 5955365	A	19990921	US 1995-480445	19950607
US 5977084	A	19991102	US 1995-480446	19950607

PRIORITY APPLN. INFO.:
US 1992-864876 A 19920403
US 1992-913669 A 19920714
EP 1993-909508 A3 19930405
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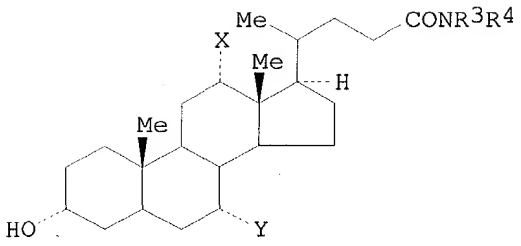
OTHER SOURCE(S): MARPAT 120:184644
GI



I

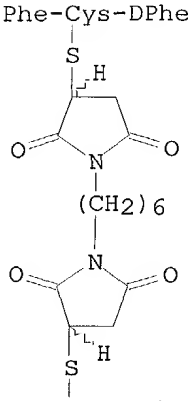
AB A self-assembling polynucleotide delivery system comprising components which aid in the delivery of the polynucleotide to the desired site which are assocd. by noncovalent interactions with the polynucleotide is described. The components of the system include DNA masking substances, cell recognition substances, charge neutralization and membrane permeabilization substances, and subcellular localization substances. The membrane permeabilization substance may be a cationic bile salt I (X,Y=H,OH; R3=H,C1-10 alkyl or alkylamine; R4=pos. charged linear/branched C1-30 alkyl or alkylamine). The DNA masking substance may be glycerol deriv. The bonding of the components to the DNA may also be mediated by intercalating agent deriv. Synthesis of galactosyl-**linked** bis-acridines or pos.-charged peptide-**linked** bis-acridines was described. Complexes of DNA with these compds. were used to transform mammalian cells.

L18 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:117549 HCAPLUS
DOCUMENT NUMBER: 118:117549
TITLE: Bradykinin antagonists
INVENTOR(S): Cheronis, John C.; Blodgett, James K.; Whalley, Eric T.; Eubanks, Shadrach R.; Allen, Lisa Gay; Nguyen Khe Thanh
PATENT ASSIGNEE(S): Cortech, Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217201	A1	19921015	WO 1992-US2431	19920330
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2106677	AA	19921002	CA 1992-2106677	19920330
AU 9218751	A1	19921102	AU 1992-18751	19920330
AU 660683	B2	19950706		
EP 586613	A1	19940316	EP 1992-917400	19920330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
HU 65328	A2	19940502	HU 1993-2780	19920330
JP 06508116	T2	19940914	JP 1992-510219	19920330
US 5416191	A	19950516	US 1993-2684	19930108
NO 9303508	A	19930930	NO 1993-3508	19930930
US 5620958	A	19970415	US 1994-227184	19940413

US 5635593 A 19970603 US 1995-440352 19950512
PRIORITY APPLN. INFO.: US 1991-677391 A 19910401
US 1992-859582 A 19920327
WO 1992-US2431 A 19920330
US 1994-227184 A1 19940413
OTHER SOURCE(S): MARPAT 118:117549
GI

DArg-Arg-Pro-Hyp-Gly-Phe-Cys-DPhe-Leu-Arg



DArg-Arg-Pro-Hyp-Gly-Phe-Cys-DPhe-Leu-Arg

AB Bradykinin antagonists are modified for increased potency and/or duration of action. The modification is done by joining a bradykinin (BK1) receptor antagonist with a BK2 antagonist or (.mu.-)opioid receptor agonist or a neuropeptide receptor antagonist through a **linker,** such as a bissuccinimidoalkane. CP-0127 (I) was prepd. by dimerized the monomer peptide CP-0126 in bismaleimidohexane. I (9 nmol/kg/min; i.v.) totally inhibited in the rat the blood pressure response to bradykinin (4 .times. 10-9 mol), whereas the parent peptide showed little activity.

L18 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:214884 HCAPLUS
DOCUMENT NUMBER: 116:214884
TITLE: A new class of bradykinin antagonists: synthesis and in vitro activity of bissuccinimidoalkane peptide dimers
AUTHOR(S): Cheronis, John C.; Whalley, Eric T.; Nguyen, Khe T.; Eubanks, Shad R.; Allen, Lisa G.; Duggan, Matthew J.; Loy, Sharon D.; Bonham, Kathryn A.; Blodgett, James K.
CORPORATE SOURCE: Cortech, Inc., Denver, CO, 80221, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(9), 1563-72
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A systematic study on the dimerization of the bradykinin (BK) antagonist H-D-Arg0-Arg1-Pro2-Hyp3-Gly4-Phe5-Ser6-D-Phe7-Leu8-Arg9-OH has been performed. The first part of this study involved compds. wherein dimerization was carried out by sequentially replacing each amino acid with cysteine and **crosslinking** with bismaleimidohexane. The second part of this study utilized a series of bissuccinimidoalkane dimers wherein the intervening methylene chain was varied systematically from n = 2-12 while the point of dimerization was held const. at position 6. The biol. activities of these dimers were then evaluated on BK-induced smooth

muscle contraction in two different isolated tissue prepns.: guinea pig ileum (GPI) and rat uterus (RU). Several of the dimeric BK antagonists displayed remarkable activities and long durations of action. In addn., dimerization at position 4, 7, 8, or 9 produced dimeric analogs with markedly reduced potency. Rank order of antagonist potency as a function of dimerization position is as follows: RU, 6 > 5 > 0 > 2 > 1 > 3 .mchgt. 4, 7, 8, 9; GPI, 6 > 5 > 3 > 2 > 1 > 0 .mchgt. 4, 7, 8, 9. Evaluation of the **linker** length as represented by the no. of methylene units indicated an optimal distance between the two monomeric peptides of 6-8 methylene moieties. These studies also revealed that the carbon-chain length significantly affected the duration of action in vitro and displayed partial agonism effects when n > 8. The optimum activity in vitro was achieved with dimerization at position 6 and n = 6 (CP-0127). Similar effects in potency were also seen when the monomeric antagonist H-D-Arg0-Arg1-Pro2-Hyp3-Gly4-Phe5-Ser6-D-Phe7-Phe8-Arg9-OH (NPC-567) was dimerized using similar chem. These results suggest that the development of BK antagonists of significant therapeutic potential may be possible using a dimerization strategy that can overcome the heretofore limiting problems of potency and in vivo duration of action found with many of the BK antagonists in the literature.

L18 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:35949 HCAPLUS
DOCUMENT NUMBER: 116:35949
TITLE: N-(3,5-Dichlorophenyl)succinimide nephrotoxicity: evidence against the formation of nephrotoxic glutathione or cysteine **conjugates**
AUTHOR(S): Rankin, Gary O.; Shih, Hsien Cheng; Teets, Vonda J.; Yang, David J.; Nicoll, Derek W.; Brown, Patrick I.
CORPORATE SOURCE: Sch. Med., Marshall Univ., Huntington, WV, 25755-9310, USA
SOURCE: Toxicology (1991), 68(3), 307-25
CODEN: TXCYAC; ISSN: 0300-483X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The agricultural fungicide N-(3,5-dichlorophenyl)succinimide (NDPS) induces nephrotoxicity via .gtoreq.1 metabolites. The possibility that a glutathione or cysteine **conjugate** of NDPS or an NDPS metabolite might be the penultimate or ultimate nephrotoxic species was studied. In 1 set of expts., male rats were administered i.p. NDPS 1 h after pretreatment with the .gamma.-glutamyltranspeptidase inhibitor AT-125 (acivicin) and renal function was monitored at 24 and 48 h. In general, AT-125 pretreatment had few effects on NDPS-induced nephropathy. In a 2nd set of expts., rats were treated i.p. or orally with a putative glutathione [S-(2-(N-3,5-dichlorophenyl)succinimidyl)glutathione (NDPSG)], a cysteine [S-(2-(N-3,5-dichlorophenyl)succinimidyl)cysteine (NDPSC) (as the Me ester)] or N-acetylcysteine [S-(2-(N-3,5-dichlorophenyl)succinimidyl)-N-acetylcysteine] **conjugate** of NDPS and renal function was monitored at 24 and 48 h. An intramol. cyclization. product of NDPSC, 5-carbomethoxy-2-(N-(3,5-dichlorophenyl)carbamoylmethyl)-1,4-thiazane-3-one was also examd. for nephrotoxic potential. None of the compds. produced toxicol. important changes in renal function or morphol. The in vitro ability of the **conjugates** to alter org. ion accumulation by cortical slices was also examd. All of the **conjugates** tested caused a redn. in p-aminohippurate accumulation at a **conjugate** bath concn. of 10-4M, but none of the **conjugates** reduced Et4N+ uptake. In a 3rd expt., the ability of the cysteine **conjugate** lyase inhibitor aminooxyacetic acid (AOAA) to alter the nephrotoxicity induced by 2 NDPS metabolites, N-(3,5-dichlorophenyl)-2-hydroxysuccinimide (NDHS) or

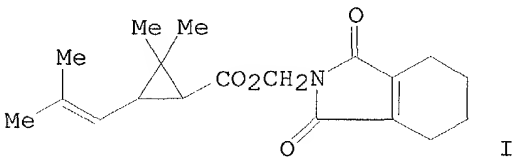
N-(3,5-dichlorophenyl)-2-hydroxysuccinamic acid (NDHSA) was examd. AOAA pretreatment had no effect on NDHS- or NDHSA-induced nephrotoxicity. These results do not support a role for a glutathione or cysteine **conjugate** of NDPS or an NDPS metabolite as being the penultimate or ultimate nephrotoxic species.

L18 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:456363 HCAPLUS
DOCUMENT NUMBER: 107:56363
TITLE: Role of dehydropeptidase-I in the metabolism of glutathione and its **conjugates** in the rat kidney
AUTHOR(S): Hirota, Takashi; Nishikawa, Yuko; Komai, Toru; Igarashi, Takashi; Kitagawa, Haruo
CORPORATE SOURCE: Anal. Metab. Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
SOURCE: Research Communications in Chemical Pathology and Pharmacology (1987), 56(2), 235-42
CODEN: RCOCB8; ISSN: 0034-5164
DOCUMENT TYPE: Journal
LANGUAGE: English
AB [14C]N-Ethylmaleimide-S-cysteinylglycine was used to investigate the role of dehydropeptidase-I in the metab. of glutathione **conjugates**. The dipeptide was rapidly hydrolyzed to [14C]N-ethylmaleimide-S-cysteine in isolated rat renal cells, and subsequently acetylated to [14C]N-ethylmaleimide-S-N-acetylcysteine. Cilastatin, a specific inhibitor of dehydropeptidase-I, strongly inhibited the hydrolysis of the dipeptide by the isolated cells. In rat kidney homogenates, the marked inhibitory effect of cilastatin was also obsd. on the hydrolysis of cystinyl-bis-glycine and leukotriene D4, which are dipeptide intermediates in the biotransformation of GSSG and endogenous glutathione **conjugate**, resp. In contrast, the inhibitory effect of bestatin, a potent inhibitor of aminopeptidase-M, was much smaller than that of cilastatin on the hydrolysis of these dipeptides by the renal cells and homogenates. Apparently, dehydropeptidase-I plays a more important role in the metab. of glutathione and its **conjugates** than aminopeptidase-M does.

L18 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:434980 HCAPLUS
DOCUMENT NUMBER: 107:34980
TITLE: Chloroacetanilide herbicide selectivity: analysis of glutathione and homoglutathione in tolerant, susceptible, and safened seedlings
AUTHOR(S): Breaux, E. Jay; Patanella, James E.; Sanders, Ernest F.
CORPORATE SOURCE: Monsanto Agric. Co., St. Louis, MO, 63167, USA
SOURCE: Journal of Agricultural and Food Chemistry (1987), 35(4), 474-8
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chloroacetanilide herbicide tolerance is due to **conjugation** with glutathione (GSH; Glu-Cys-Gly) or homoglutathione (hGSH; Glu-Cys-.beta.-Ala). New anal. methods were developed and used to analyze these tripeptide thiols in plants. These methods are based on the selective derivatization of these detoxification thiols with radiochem. labeled maleimides such as N-ethylmaleimide. The maleimide adduct derivs. were then sepd. by reversed-phase HPLC and quantitated with the aid of a radiochem. HPLC detector. By these new methods it was found that

chloroacetanilide herbicide tolerance was related to the seedling detoxification thiol content. Also, the herbicide safener flurazole caused the level of GSH to increase in the shoots of treated corn and sorghum.

L18 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:194769 HCAPLUS
DOCUMENT NUMBER: 96:194769
TITLE: Glutathione **conjugate** of the pyrethroid tetramethrin
AUTHOR(S): Smith, Ian H.; Wood, Edgardo J.; Casida, John E.
CORPORATE SOURCE: Dep. Entomol. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Agricultural and Food Chemistry (1982), 30(3), 598-600
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB tetramethrin (I) [7696-12-0] and its cleavage product tetrahydrophthalimide [4720-86-9] readily undergo Michael addn. with thiols. In the case of GSH [70-18-8] the resulting I GSH **conjugate** [**80603-64-1**] is less stable than the mercapturic acid **conjugates** of I and tetrahydrophthalimide. The I GSH **conjugate** is formed under physiol. conditions in the presence of mouse liver and housefly abdomen homogenate fractions but probably as a nonenzymic reaction. The mouse liver sol. thiol level is diminished by i.p. administration of tetrahydrophthalimide. Mercapturic acid and GSH **conjugates** of I are not evident in the bile or urine of i.p.-treated rats and mice. Although **conjugation** with GSH is not a significant factor in the metab. of I, it is interesting to speculate that reversible Michael addn. with a crit. thiol in the pyrethroid receptor site might contribute to the unique potency and transient character of the neuroactivity of I.

L18 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:564304 HCAPLUS
DOCUMENT NUMBER: 95:164304
TITLE: Asymmetry of lipid dynamics in human erythrocyte membranes studied with impermeant fluorophores
AUTHOR(S): Cogan, Uri; Schachter, David
CORPORATE SOURCE: Coll. Physicians and Surg., Columbia Univ., New York, NY, USA
SOURCE: Biochemistry (1981), 20(22), 6396-403
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis, purifn., and application of 5 membrane-impermeant derivs. of pyrene are described. Each probe consists of a membrane-impermeant

moiety, either an oligosaccharide or gluthathione, **linked** to pyrene via a connecting arm. Intact human erythrocytes and leaky ghost membranes prepd. from them were treated with the probes to label, resp., the outer membrane leaflet and both leaflets. Motional freedom of the pyrene fluorophores in the membrane was assessed by estn. of the steady-state polarization of fluorescence, the excited-state lifetime, and the excimer/monomer fluorescence intensity ratio. The fluorescence anisotropy of each impermeant deriv. was lower in the outer as compared to the inner hemileaflet, whereas the corresponding excited-state lifetimes were similar. Excimer formation was consistently greater in the outer leaflet. Thus, the impermeant fluorophores experience greater motional freedom (fluidity) in lipid domains of the outer as compared to the inner leaflet of the human erythrocyte membrane.

L18 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:38065 HCAPLUS
DOCUMENT NUMBER: 70:38065
TITLE: Acylation reactions with cyclic imides
AUTHOR(S): Smyth, Derek G.; Tuppy, Hans
CORPORATE SOURCE: Nat. Inst. Med. Res., Mill Hill, UK
SOURCE: Biochimica et Biophysica Acta (1968), 168(2), 173-80
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Maleimide reagents were examd. for a potential use in the **crosslinking** of amino and thiol groups in proteins. The adducts obtained by reaction of N-ethylmaleimide or of N-(4-dimethyl-3,5-dinitroaminophenyl)maleimide with cysteine, homocysteine, and glutathione were prepd. and the rates of reaction of the imide rings with water and with amino groups were studied. In the cysteine-maleimide addn. products, where amino and thiol groups are located in positions sterically favorable for cross-**linking**, intramol. aminolysis occurs readily. In contrast, the amino group of the homocysteine and glutathione adducts is comparatively stable.